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JEJUNOSTOMY FOR THE RELIEF OF MALFUNCTIONING GASTROENTEROSTOMY STOMA

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OBSTRUCTION at the anastomatic stoma following gastroenterostomy or gastric resection occurs with considerable frequency and is a very serious complication. Numerous contributions have appeared in the literature attempting to explain its origin; yet, the cause is variable and usually not evident. Obstruction, therefore, cannot be prevented with certainty and, when it appears, the surgeon must treat it promptly and correctly to avoid a fatal outcome. Since we have had to deal with this complication so often, we believe it is worth while to record our experiences with the method of treatment that we have found to be most satisfactory.

Since postoperative obstructions should theoretically be relieved by correcting the cause or prevented by avoiding certain pitfalls, some attention must be paid to the various known ways by which obstruction may be produced. *Mechanical deficiencies* in the anastomosis occasionally cause malfunction. One of the loops of intestine may be twisted so that an actual kink is made. Sutures uniting the transverse mesocolon to the stomach above the line of anastomosis may give way or not be properly placed, allowing a segment of small bowel to herniate through the open trap. The position of the anastomosis, the direction of the opening in the stomach wall, the question of an iso- or retroperistaltic direction of the jejunal loop, and the length of the proximal limb of jejunum have all been more or less settled by laboratory data and clinical experience. The usual method in use in our clinic is a short loop anastomosis with proximal jejunum sutured to the lesser curvature in a more or less vertical direction at the junction of the middle and lower thirds of the stomach. Posterior anastomoses have been more popular than anterior, both with gastroenterostomy and following partial gastrectomy. The use of lightweight rubber-covered clamps has been the

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routine, since years ago it was felt that heavier clamps, on occasion, did cause thrombosis of blood vessels with subsequent edema and malfunction. Two layers of fine chromicized catgut have been used in most of the cases; some have had three rows of catgut and a few anastomoses have been done with interrupted fine silk. Increasing experience has diminished the number of mechanical obstructions so that, in the series we are reporting, only one patient could be considered to have suffered from any technical error at the time of the original operation.

Adhesions associated with a plastic peritonitis of low grade near the suture line have frequently been considered a cause for malfunction of the stoma. They are present, however, to some extent in nearly every case and, since some stomachs empty completely in spite of them, it offers a poor explanation for the anastomoses that do not function at all. In other words, it seems obvious to us that this is not often, if ever, the sole cause of trouble. We must include here the possibility of a dense adhesion between a segment of small bowel and the region of the anastomosis or raw fatty edge in the transverse mesocolon opening. Such could obstruct the bowel at the level of the adhesion and without herniation. This makes it necessary to re-explore the abdomen at the time of jejunostomy to avoid overlooking this rare cause for obstruction.

Acute dilatation of the stomach distorting the anastomosis is now practically unknown, due to the routine use of the Levine tube. The tube is inserted before the operation and left in place for forty-eight to seventy-two hours afterwards. Its removal is dependent upon evidence of an adequately functioning anastomosis. Atonia of the stomach has also been blamed as a cause for its failure to empty. This is not uncommon, especially in the patient who has had a long period of preceding obstruction before the primary operation on the stomach. Such a patient may clear up his obstruction remarkably on a highly seasoned solid diet, when all previous efforts had resulted in persistent lack of peristalsis.

Biochemical Factors.—The most tenable theory is that elaborated by Ravdin.[1] He believes obstruction of the anastomosis is due to edema and emphasizes, with Jones and Eaton,[2] the importance of subclinical states of hypoproteinemia in the production of edema and malfunction. We agree that obstruction is probably often due to edema in the region of the stoma. However, the serum protein measured in the usual fashion is normal in most of the patients with the complication under discussion.

Despite these numerous theories, the actual situation found at secondary operation is apt to reveal no satisfactory explanation of the difficulty. Preoperative studies will usually show blood chemistry determinations to be within normal limits. At laparotomy, the stomach will be found to be small and not distended. A few loose adhesions will usually be seen about the anastomosis, but they rarely can be considered to have any bearing on the situation. The surgeon may well be perplexed, since he has operated for a very serious complication and has

found nothing to explain it satisfactorily. However, numerous procedures to correct the fault are available. *Enteroenterostomy* between the afferent and efferent loops of jejunum was a favorite procedure in earlier years. It involves, however, many difficulties. Plastic adhesions about the anastomosis have to be broken up in order to identify the exact segments of jejunum. When a short loop posterior anastomosis has been made, the length of the afferent portion of jejunum may be too short to perform this operation satisfactorily. Enteroenterostomy in cases of duodenal ulcer carries the hazard of marginal ulcer after the patient has recovered from his original operation. For this reason alone, we believe it should never be done except when dealing with carcinoma associated with achlorhydria.

A second gastroenterostomy is another procedure that has been employed. If the original anastomosis has been placed posteriorly, an anterior gastroenterostomy is tried. The obstruction tends to recur in the new anastomosis from the same factors that caused it in the primary stoma. It is only of value in case there has been some actual mechanical misadventure at the time of the original gastroenterostomy.

Duodenojejunostomy has been performed to relieve malfunction, uniting the third portion of the duodenum to the descending loop of jejunum. This is accomplished after the duodenum is exposed through the transverse mesocolon. It may be a difficult operation and is open to exactly the same objections as an enteroenterostomy.

Gastrostomy was a favorite procedure of some of the continental surgeons before the Levine tube became popularized; this took the tension off an overloaded stomach and allowed edema to subside and the anastomosis to function. Some authorities, such as Perman,[3] have considered this operation to be the most satisfactory method of dealing with obstruction.

It has been suggested that postoperative obstruction will not occur if an inlying tube of the Abbott-Rawson[4] type is used, one portion of the tube being left in the stomach while the other enters the efferent loop of the jejunum extending well past the anastomosis. By this means, the stomach contents may be aspirated and immediately returned to the jejunum; also, it has the advantage that early feedings may be introduced into the jejunum. While this may be of value in some cases, the fact that when true obstruction occurs, three weeks usually elapse before the stoma reopens, means that the nasal tube would need to be retained for this long period in those very cases in which it is most desperately needed. Such continuous retention of the nasal tube is not only uncomfortable to the patient but has definite hazards, aside from an irritating pharyngitis. Iglauer and Molt[5] have reported several instances of a necrosing laryngitis requiring tracheotomy for relief. It is also very difficult to retain a nasal tube over a long period of time if the patient has any pulmonary complications at all.

Jejunoplasty has recently been proposed by Hoag and Saunders[6] as a method of treatment. This involves actual exposure of the anastomosis with a plastic procedure upon the stoma. We have had no experience with this operation. It is of considerable interest but involves a rather extensive dissection on a patient that is very ill. Follow-up studies on patients treated by this method may show that marginal ulcer will follow as frequently as it does after enteroenterostomy.

Jejunostomy has also been used extensively. It has not been a popular operation until recently. This is probably due to the fact that the inlying nasal tube was not employed in earlier years. Thus, Perman[3] found that the mortality following jejunostomy for stomal obstruction was 80 per cent in his series. The procedure, however, has evoked considerable interest in this country. Gibson[7] in 1900 performed jejunostomy as an adjunct to operations on the stomach in order that the patient might be fed at an early period. Its use in the treatment of postoperative obstruction of the stoma has been advised by Graham,[8] Walters and Hartman,[9] Pfeiffer,[10] and Clute.[11]

Jejunostomy, then, is one of the oldest operations devised for the malfunctioning stoma. Its advantages are: (1) the simplicity of the operation; (2) the fact that the gastrojejunal anastomosis is left in the exact condition that it was planned originally; (3) the fact that it effectively maintains the patient's nutrition until edema of the anastomosis subsides and obstruction is relieved. However, attention must be paid to the details and indications for this procedure in order that its application may be successful. We believe it is not jejunostomy itself, but jejunostomy that is performed according to certain indications and in a certain fashion that constitutes the best method of dealing with postoperative obstruction of the stoma.

The material from which these data have been drawn has been collected from the cases observed in the Massachusetts General Hospital from the years 1936 to 1940, inclusive. The first four cases in the series have been treated by us personally and the others by various surgeons on the staff (Table I). The actual technical procedures often varied considerably so that conclusions may be drawn with regard to the best method. We shall attempt to set down a critical analysis of our experience with this operation.

In our clinic jejunostomy has been employed as a preliminary procedure to operations upon the stomach, as a concomitant operation to gastric surgery being done at the same time, and, third, as a measure for the relief of postoperative obstruction. The performance of preliminary or concomitant jejunostomies has been urged as a measure to improve general nutrition and thus prohibit or decrease the number of postoperative complications. Preliminary jejunostomy is not without its hazards. We have found that, if the stoma is placed too low in the flank, it may constitute a fixed point about which the small intestine may herniate,

TABLE I

FREQUENCY OF POSTOPERATIVE OBSTRUCTION

TYPE OF OPERATION	OPERATIONS	JEJUNOSTOMIES	FREQUENCY OF OBSTRUCTION
Gastrojejunostomy			
Posterior	73	7	9.7%
Anterior	11	0	--
Gastric resections			
Posterior gastrojejunal anastomoses (Pólya, Billroth II, Hofmeister)	162	5	3.1
Anterior gastrojejunal anastomoses (Pólya, Hofmeister)	24	1	4.1
Gastroduodenal anastomoses (Billroth I, gastroduodenostomy)	7	2	29.0
Pyloroplasty	5	0	--
Total	282	15	5.3

producing intestinal obstruction. Jejunostomy performed in the Witzel fashion has actually been found to have obstructed the portion of small intestine proximal to it. Also, it requires usually about three weeks of jejunostomy feeding before any actual improvement can be noted in the patient's general condition. Often one cannot measure this improvement since the laboratory findings and weight chart may remain unchanged. There can be no doubt that such patients do withstand a large resection better if the ingestion of food has been interfered with for some time before. It probably should be used with greater frequency.

Concomitant jejunostomies have been used almost routinely with total gastrectomies in our clinic and occasionally in patients who appear to be poor operative risks from prolonged starvation. Further experience may show that we should employ it more often than we do now. It prolongs the operating time only a few minutes and often shortens the convalescence materially.

It is possible that the number of postoperative jejunostomies may be diminished by attention to the special patients who are likely to develop obstruction; in such cases jejunostomy should be done concomitantly with the original operation. Thus, the percentage of obstruction following posterior gastroenterostomy is considerably higher than it is following resection of the stomach. Patients with thick fat mesocolons are prone to develop obstruction, especially if the posterior anastomosis is employed. Secondary operations, as for stomal ulcer, carry more hazard if the mesentery of the jejunum is very short so that an anterior anastomosis cannot be made. Placing the new anastomosis through the unavoidably scarred and traumatized opening in the mesocolon is conducive to malfunction. Such patients may do well to have a jejunostomy at the time of the original operation.

Assuming that operation has been performed and jejunostomy has not been done, the patient must be carefully observed for any signs of

postoperative obstruction. The inlying nasal tube is allowed to drain by gravity and is aspirated at least every two hours. The patient is given nothing by mouth on the day of operation, an ounce of water an hour on the next, and two ounces on the second day. The fluid taken in by mouth is carefully noted and compared with the amount that is aspirated from the Levine tube. If the amount swallowed exceeds that withdrawn, the gastric balance is said to be positive; on the other hand, if the patient puts out more fluid through his nasal tube than he takes by mouth, his gastric balance is said to be negative. In the usual case, there is a slight negative balance of 100 to 200 c.c. during the first forty-eight hours; the balance then becomes positive and remains so. Patients who are to develop obstruction will often show

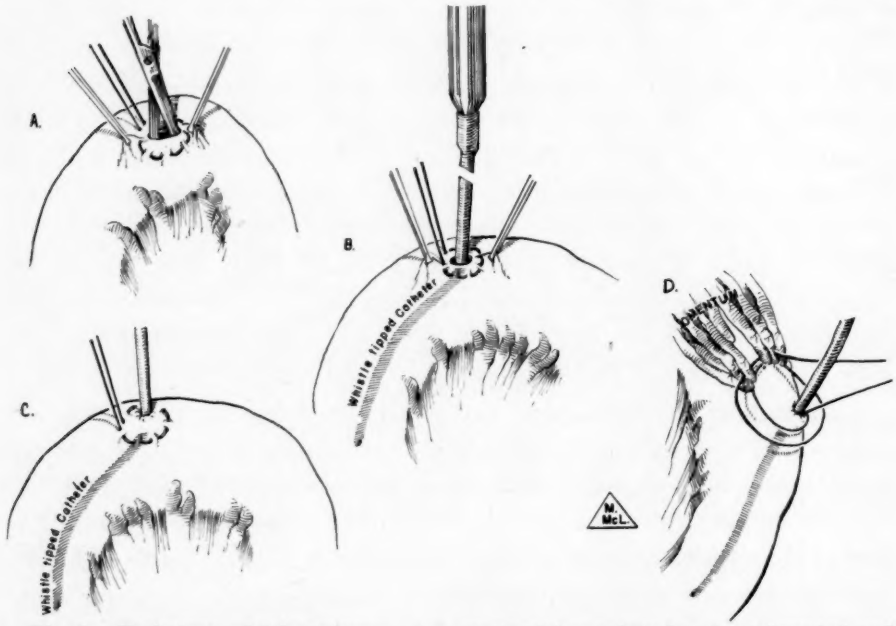

Fig. 1.—Technique of jejunostomy: *A*, a purse-string suture has been inserted and the jejunum is opened with scissors. *B*, the catheter is inserted, passage being facilitated by introduction of saline solution through a syringe. *C*, a second purse-string suture is made. *D*, omentum is brought about the tube.

as great a negative balance as 1,000 c.c. on the first postoperative day. This immediate obstruction is by far the most common type. Other patients soon have a positive balance; the nasal tube is withdrawn at the usual time and then suddenly on some later day obstruction is discovered. The sixth to the eighth day is the most common time for delayed obstruction to appear; however, it must be emphasized that signs of obstruction usually date from the time of the original operation. Its presence is often clouded by clinical optimism or by failure to employ daily aspirations to test the gastric residual.

If the gastric balance is negative and obstruction is definitely present, it is wise to watch the patient for a short period of time. Many patients will have only a small negative balance for a few days, in-

dicating that a large proportion of the gastric contents are passing through the anastomosis. In such cases, further conservative therapy is indicated. Other patients run a negative balance from 1,000 to 3,000 c.c. daily; they should be regarded as completely obstructed and reoperation is indicated at an early date. Long-continued negative balances, even though they be small in amount, are likewise extremely dangerous and often must be corrected by reoperation. From a study of our cases, we have obtained the impression that the great danger is the omission of this operation until too late. The hazard does not lie in the procedure itself but in delay, during which time the patient's resistance is lowered and he becomes prey to other complications. Thus, patients dying of late obstruction die of pulmonary complications as a general rule; they must be regarded as much poorer risks than their general condition indicates or than their blood chemistry tests may show.

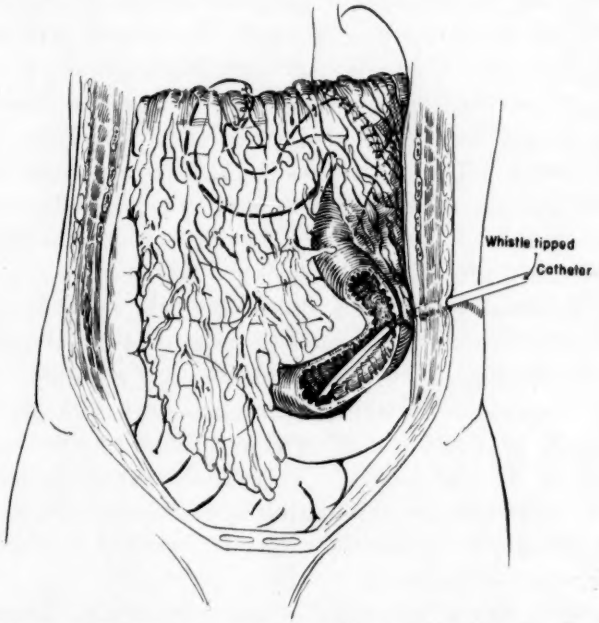

Fig. 2.—Diagram illustrating the final position of the jejunostomy catheter.

To wait until the patient actually needs the jejunostomy to maintain his general condition is to wait too long. This is especially true in the older age group. The mortality of obstruction in the patients whose age is 50 years or over is nearly 50 per cent, while none in this series have succumbed to that complication who were under the age of 50 years. In addition, all patients above 50 years of age who had reoperation before ten days of obstruction had elapsed recovered; while of the five patients who had reoperation after ten days or more of obstruction, there was only one recovery. With the younger age group in whom resistance is higher, operation can be deferred for a comparatively long period of time without fatal outcome. We believe that reoperation should be done in the older age group a week after obstruction has oc-

curred, while with those patients under 50 years of age it may be deferred for a few more days if the patient is in good condition and if there are clinical and laboratory data that offer hope of further improvement.

It is sometimes desirable to prove the diagnosis of obstruction by the oral administration of a little barium followed by fluoroscopic observation. The barium usually passes slowly through the anastomosis and then entirely stops about one inch below the stomach in the region of the efferent loop. Occasionally under the fluoroscope one may find that a certain posture enhances the passage of stomach contents into the efferent jejunal limb and, by utilizing this position after feedings, the situation will gradually clear up.

When reoperation is performed, certain technical details are extremely important. Spinal anesthesia, evipal, or local novocain block may be used. An adequate incision is necessary. We believe the best approach may be gained by reopening the previous operative wound. This will allow inspection of the anastomosis and elimination of any mechanical cause of nonfunction. Correction of such a mechanical cause, if found, should be supplemented by a jejunostomy. Plastic adhesions about the anastomosis should not be divided since they will only re-form in a more dense fashion. The efferent loop of jejunum should be accurately identified and visualized over a distance of 18 inches below the site of the anastomosis. It must be ascertained that there are no bands obstructing the intestines below this point.

The most common errors of jejunostomy will have been avoided by these details. Often one is tempted to wait until the patient is in such precarious condition that he will stand no other anesthesia than a little novocain in the abdominal wall. Through a tiny subcostal incision, an attempt is made to define the efferent loop; it is usually impossible and a tube is placed in a portion of the jejunum that may be entirely unsatisfactory. One case in this series had definite obstruction from a point below the site at which the tube was inserted so that the jejunostomy did more harm than good.

The loop of jejunum selected for insertion of the tube must be one that will lie comfortably just beneath the left costal margin in the nipple line without any tension on either the upper or lower limbs; usually this is about twelve inches below the anastomosis. The site selected for the stab wound must not be too low or too near the midline, since the small bowel may rotate about the fixed point if the intestine is carried away from its natural position. The jejunum is carefully protected by moist gauze packs and a purse-string suture of No. 00 chromic catgut is introduced. The jejunum is then opened at this spot and a No. 16 French whistle-tipped catheter inserted. The tip of the catheter must point distally down the jejunum. It is extremely easy to direct it the opposite way unless care is taken. Introduction of the catheter is often facilitated by the gentle insertion of normal salt solution through the catheter with an asepto syringe during the time the tube

is being inserted into the bowel. After six inches of the catheter have been placed within the jejunum, the purse-string suture is tightened and then carried through the wall of catheter to anchor it in position. This first suture is then buried by a second inverting purse-string suture placed about the catheter not more than one-fourth inch outside of the original. The catheter is then brought through a small opening which is made in the great omentum and out through the stab wound in the left subcostal area. There should be no kinking of the jejunum at the time the abdomen is closed. We have tried bell-tipped catheters for jejunostomy and given them up since they have no advantage over the whistle-tipped tube and on one occasion at least failed to function due to compression of the flange by the purse-string suture.

We have found this to be a much more satisfactory procedure than the Witzel type of jejunostomy. The Witzel method in a bowel of normal size will reduce its lumen quite markedly so that the added edema of operation may produce subacute obstruction. This occurrence has been noted occasionally in patients on whom this type of jejunostomy was done as a preliminary procedure to gastric resection. The Witzel jejunostomy is also more difficult and time consuming to perform. It possesses no advantages over the simple purse-string jejunostomy. Following the removal of the catheter in either type, leakage from the abdominal sinus will cease almost immediately.

Following the jejunostomy, the surgeon is then committed to what may seem to him to be an interminable period of waiting until the edema about the original anastomosis subsides and stomal obstruction is relieved. During this period, he will probably attempt many variations of the oral intake in an attempt to relieve the obstruction. However, relief is a matter of time rather than any other factor. The surgeon must possess the courage to realize this fact and to persist until obstruction is finally overcome. In our cases this has occurred any time from fourteen to fifty days after the resection. The average length of time after jejunostomy before obstruction is relieved is twenty-two days in this series.

It is important that the patient's nutrition be maintained during this period of time and the stomach kept empty by an inlying nasal tube. If the nasal tube becomes uncomfortable, repeated gastric aspirations may be employed instead. The matter of feeding through the jejunostomy tube in our experience has been a totally individual problem. No one diet that can be specified for one person is apt to be satisfactory for another. There are a few features that are important, however. The first is that so far as possible it is wise to return the contents aspirated from the stomach into the jejunum. Occasionally, at certain stages, it may be possible to allow the patient to have a certain amount of food by mouth, withdraw the partially digested contents, and return them to the jejunum. In the early stages of feeding, milk and lime water mixed in equal parts are usually best tolerated. Saline solution often starts a

severe diarrhea; this may be avoided by the use of tap water as a basis for any feedings that are employed. After the jejunum tolerates simple liquids, the caloric intake may be increased and varied.[12] Any suitable food that can be divided finely enough to be forced through the tube can be given. The exact diet is quoted in one of the cases cited at the end of this article in order that its variegated nature may be apparent. Any tendency to diarrhea is easily controlled by an occasional teaspoonful of paregoric inserted in the jejunostomy tube or added to the feedings. We formerly used tincture of opium for this purpose, but paregoric as suggested to us by Graham[8] is more effective. The urinary output can be kept at a satisfactory level usually by the jejunostomy feedings; if, however, it is not adequate, intravenous saline solution can be used.

Frequent determinations must be made of the blood chemistry. The nonprotein nitrogen has remained normal in about half our cases, but in the other half has risen appreciably. In certain cases this has definitely been the effect of an underlying chronic nephritis; in others the nonprotein nitrogen seems to have risen for no apparent reason. The serum protein will usually require maintenance by means of repeated transfusions, although after protracted jejunostomy feedings sufficient protein may be acquired in this fashion to maintain an adequate level. The serum chloride will often be found to fluctuate and this again can be easily controlled by means of either intravenous saline solution or distilled water, as the case may indicate.

Patency of the stoma may finally be determined by use of the barium meal. As soon as the gastric balance becomes positive, improvement is extremely rapid. The jejunostomy tube is usually removed a few days after the gastric balance is satisfactory. After the patient has definitely improved, it is well to withhold jejunostomy feedings for twelve hours periodically. Unless this is done, one may find the stoma widely open and ready for mouth feedings in spite of an apparent negative balance. This is explained in two ways: some of the jejunostomy feedings regurgitate into the stomach and are withdrawn through the Levine tube; also, there must be a physiologic need for food to pass through the stoma and the upper jejunum must be empty before this need asserts itself.

The cases that we have treated by jejunostomy are summarized in Table II and are abstracted briefly at the conclusion of this article. We have found that obstruction, which is first noted immediately after operation and in which a negative gastric balance continues from that time on, is the most serious type. On the other hand, those cases in which the gastric balance is first positive for six to eight days and obstruction then follows have a comparatively good prognosis. Patients with immediate complete obstruction will practically always require a jejunostomy for relief at an early date if they are to survive. If the obstruction develops late, conservative procedures, such as repeated gastric aspirations and a reduction in the fluid intake by mouth,

TABLE II*

NO.	AGE	DATE OF OBSTRUCTION	DATE OF JEJUNOSTOMY	DURATION OF OBSTRUCTION BEFORE JEJUNOSTOMY	DATE OF RELIEF OF OBSTRUCTION	DISEASE†	OPERATION	RESULT
1. C. H.	45	6th day	12th day	6 days	42nd day	D. U.	Resection, posterior Hofmeister	Lived
2. F. B.	42	Immediately	8th day	8 days	30th day	D. U.	Posterior gastroenterostomy	Lived
3. R. C.	64	Immediately	9th day	9 days	25th day	D. U.	Posterior gastroenterostomy	Lived
4. F. K.	51	Immediately	5th day	5 days	14th day	D. U.	Posterior gastroenterostomy	Lived
5. C. H.	66	8th day	14th day	6 days	50th day	D. U.	Resection, anterior Hofmeister	Lived
6. M. B.	24	(?) Immediately	15th day	15 days	32nd day	G. U.	Resection, Billroth I	Lived
7. S. S.	70	Immediately	5th day	5 days	31st day	Ca. stomach	Posterior Pólya resection	Lived
8. H. B.	50	Immediately	7th day	7 days	26th day	D. U.	Resection, Billroth I	Lived
9. S. B.	34	Immediately	13th day	13 days	31st day	D. U.	Posterior gastroenterostomy	Lived
10. M. D.	74	Immediately	15th day	15 days	27th day	Ca. stomach	Posterior gastroenterostomy	Lived
11. J. A.	62	10th day	15th day	5 days	25th day	Ca. stomach	Posterior Pólya resection	Lived
12. G. L.	59	Immediately	15th day	15 days	———	Ca. stomach	Posterior Pólya resection	Died
13. W. I.	70	4th day	16th day	12 days	———	Ca. stomach	Posterior Pólya resection	Died
14. C. C.	60	Immediately	17th day	17 days	———	D. U.	Posterior gastroenterostomy	Died
15. J. L.	60	6th day	17th day	11 days	———	D. U.	Posterior gastroenterostomy	Died

*Dates are all estimated from day of original operation.
†*D. U.*, duodenal ulcer; *G. U.*, gastric ulcer; *Ca.*, carcinoma.

will often produce relief without the necessity of surgery. Two or three days of conservative treatment are often enough in the latter group, but not over a week of obstruction should be allowed to pass before a jejunostomy is done. It is impossible to estimate accurately from our records the number of patients who have a mild temporary obstruction from which they recover without surgery. It is our impression that about as many patients are treated in a conservative fashion as require reoperation. In all of these mild cases there has been no prolongation of the usual hospital stay and in only a few of them were symptoms marked enough to require any notation in the progress notes. No deaths occurred in this group in which obstruction could have conceivably played a role.

On the other hand, all the severe forms of obstruction were treated by reoperation. All of the reoperated cases, with one exception, had a jejunostomy performed and are summarized in the clinical abstracts. The other case recovered after an enteroenterostomy, a complete kink of the efferent loop having been found at reoperation. This is the group which, according to Hoag and Saunders,[6] has an expected mortality of 60 to 75 per cent.

In our series of 15 cases treated by jejunostomy, 5 patients had carcinoma of the stomach, while 10 had an ulcer, of which 9 were duodenal and 1 gastric. Half of the obstructions followed posterior gastroenterostomy. Five followed resections with posterior anastomoses (4 Pólya, 1 Hofmeister), 1 followed resection and an anterior anastomosis of the Hofmeister type, and 2 followed a Billroth I procedure. When comparison is made with the number of these operations done in the clinic during the same period, it is shown that in this series gastroenterostomy was definitely more likely to be followed by obstruction than were the resections with posterior anastomoses. In our series of gastric operations in the last five years about 1 patient out of 10 developed obstruction following a posterior gastrojejunostomy, while about 1 out of 30 had the same complication after resection and posterior anastomosis. The frequency of postoperative obstruction, therefore, has been three times greater after posterior gastroenterostomy. Our experience with anterior anastomoses either of the Hofmeister or Pólya has not been extensive, but obstruction does not appear to be less common. This is due, in part, to the use of anterior anastomoses in certain cases described above in which posterior anastomosis would have been almost sure to cause obstruction. It is interesting that the number of postoperative obstructions following the few Billroth I resections were comparatively high; this has been emphasized frequently in the literature.

Ten of the patients had definite negative gastric balances beginning on the first postoperative day and continuing thereafter until operation was performed. Five of the patients in whom the obstruction developed at a later period required jejunostomy.

In the group of patients 50 years of age or under, there were no postoperative deaths. All of them had ulcer. The secondary operation was performed from five to fifteen days after obstruction had been noted. In other words, it seems that the young patients are comparatively good risks and will occasionally tolerate a long period of obstruction.

Ten of the patients were over 50 years of age; 5 of them had ulcers and 5 had cancers of the stomach. Two of the ulcer patients and 2 of the cancer patients died. The ultimate result then did not seem to depend so much on the underlying disease as it did on the fact that of the patients who had the jejunostomy performed under less than ten days after the obstruction began none died; while of those patients who had it delayed over ten days, all succumbed with one exception. The length of time the obstruction persisted after jejunostomy was done seemed to bear little relation to the date that obstruction first occurred. In other words, while late obstruction is usually mild, it can be fully as persistent as the immediate type.

Summary.—Early postoperative gastric obstruction following gastroenterostomy or gastric resection is due, in nearly every case, to edema in the region of the stoma. Relief may be secured in several ways, but, if the patient can be kept alive and in good physical condition for a period that has varied from fourteen to fifty days in our series, the edema will subside and obstruction be relieved. The operation of choice for this complication is jejunostomy. It has been required for postoperative obstruction 15 times in a series of 282 gastric operations in the past five years in this hospital. Mild obstructions occur nearly as frequently but subside promptly and carry no mortality.

Large negative gastric balances beginning immediately after operation usually mean that reoperation will be necessary. Persistent negative balances, even if they are small, are nearly as dangerous. The important consideration is that the second operation be done at an early date while the patient is still in good condition. We believe that a week of obstruction is sufficient indication in patients over 50 years of age, while younger patients may be allowed a slightly further delay.

When jejunostomy is done, it should be performed through an adequate incision, preferably through the original operative wound. We advise a No. 16 French whistle-tipped catheter held in place by two closely placed purse-string sutures. The catheter is brought out through the great omentum and through a subcostal stab wound.

There were four deaths, indicating a mortality of 27 per cent in those patients obstructed severely enough to require reoperations. These four were all over 50 years of age and had had over ten days of obstruction before the jejunostomy was done.

CONCLUSIONS

1. Early postoperative obstruction of the gastroenterostomy stoma may be allowed to continue a week if the patient is over 50 years of age, or slightly longer if he is young and in good condition.

2. Reoperation is indicated if obstruction still is present at that time.

3. The most satisfactory method of treatment is jejunostomy performed through the original wound with a No. 16 French whistle-tipped catheter placed in the jejunum by a purse-string technique.

CASE HISTORIES*

CASE 1.—C. H. (P. H. No. 1312), a 45-year-old male, was admitted to the hospital on Jan. 16, 1939, because of repeated gastric hemorrhages.

Seven years before he had had a transection of the pylorus and a posterior gastroenterostomy performed by another surgeon because of a bleeding duodenal ulcer. Postoperatively, despite adherence to a rigid diet, after a respite of three years, he began to have recurrent hemorrhages. During this period several x-ray examinations were made. There was never any evidence of a gastrojejunal ulcer. The gastric rugae were prominent. The barium left the stomach very slowly through the gastroenterostomy stoma. A gastric residue was still present at the end of twenty-four hours.

He entered the hospital this time two weeks after his last hemorrhage for consideration of surgery. It was thought that his bleeding originated from hypertrophic gastritis and that his stoma was too narrow to allow regurgitation of the contents of the duodenal loop.

Examination at entry showed a well-developed and well-nourished man. He weighed 160 pounds and was in excellent general condition. The physical examination was essentially negative. His blood pressure was 120/80; his pulse, 70. The red cell count was 3,970,000; white count, 6,700; and the differential count, normal. The bleeding time was 1½ minutes. The clotting time was 7, 13, 20, and 23 minutes in four tubes. Clot retraction was normal. The blood cevitamic acid was 0.6 mg. per cent; the plasma protein, 6.5 per cent. A liver function test was normal. The stools were negative to guaiac. A gastric analysis showed 36 c.c. of 1/10 normal HCl acid and 44 c.c. of combined after a test meal of 50 c.c. of alcohol.

Another x-ray examination showed evidence of gastritis, but none of ulcer. A gastroscopy was done by Dr. E. B. Benedict. The gastroenterostomy could not be visualized. There was a marked superficial and hypertrophic postoperative gastritis with erosions and hemorrhage.

Operation was performed on Jan. 30. Dense scar tissue was found about the stoma. The gastroenterostomy was identified. It was tightly constricted by a thick, porky mesocolon, nearly 2 cm. in thickness. The stoma was found in a high position, so that the antrum formed a kind of pouch, capable of holding nearly 500 c.c. There was no evidence of residual duodenal or a gastrojejunal ulcer. The lower two-thirds of the stomach, together with the stoma, were resected. An end-to-end aseptic anastomosis of the jejunum was made. A Hofmeister type of gastrojejunostomy was performed. Although the inflamed mesocolon made a posterior anastomosis unsatisfactory, it had to be done, since a short mesentery of the jejunum precluded an antecolic procedure.

*Cases 1, 2, and 3 were mentioned briefly by the senior author (A. W. A.) in the discussion of the paper of Hoag and Saunders.[12]

The pathologic specimen measured 14 cm. along the lesser curvature and 21 cm. along the greater. The whole mucosa was covered with small ulcerations, many of which were bleeding. The microscopic report was subacute and chronic gastritis.

Postoperatively an inlying nasal tube was left in place three days. During this time he daily put back 500 to 1,500 c.c. more through the tube than he took by mouth. The tube was withdrawn and he had no distress for three more days. On the sixth postoperative day the tube was replaced, and Wangensteen suction was instituted. He continued to run a negative gastric balance of nearly 1,500 c.c. daily.

His blood chemistry remained normal. On the twelfth day, since the stoma was obviously obstructed, the abdominal wound was reopened. There was a great deal of edema and many fresh adhesions about the mesocolon. The anastomosis was intentionally not freed. Two fingers could be passed into it from above, however. A jejunostomy was made with a No. 16 Pezzer catheter about eight inches below the ligament of Treitz, bringing the tube out through a small stab wound in the left subcostal area.

Thereafter he drained about 3,000 c.c. daily of stomach and duodenal contents through his nasal tube. This liquid was all returned to his intestinal tract, together with gradually increasing quantities of food. The diet was carefully calculated by Dr. B. H. Ragle. The jejunostomy tube functioned perfectly, he had no diarrhea at any time, and he gained weight. His blood chemistry and cell counts remained at normal levels throughout the convalescence. He received a total of three transfusions, one at the time of the resection and two at the time of the jejunostomy.

Eleven days after the jejunostomy the nasal tube was removed for several hours at a time, because of increasing irritation of the throat, and a little bleeding therefrom. He had tolerated it for sixteen days at that time.

His negative gastric balance slowly diminished. Fifteen days after the second operation it was still 500 c.c. A small amount of barium was given by mouth, and a trace could be seen to pass through the anastomosis. Twenty-seven days after the jejunostomy, feedings by the jejunal tube were entirely omitted, and on the following day nothing was obtained at any time from aspiration of the stomach. On the next day, forty-two days after the original operation, barium by mouth was seen to pass rapidly through the stoma under the fluoroscope. At that time he was tolerating a soft solid diet by mouth.

The jejunostomy diet, of considerable interest in this case, may be summarized as follows: (During this time he was receiving about 60 to 90 c.c. of water hourly by mouth to prevent parotitis or irritation from the nasal tube.)

Day of jejunostomy	Nothing.
First day	All of gastric aspirations (2,000 c.c.); 1 Gm. cebione; saline solution, 1,500 c.c.; betelin, 6.6 mg.
Second day	All of gastric aspirations (3,000 c.c.); 500 c.c. milk and lime water, 2 egg whites, and beef juice, 180 c.c.
Third day	All of gastric aspirations; 4 egg whites; beef juice, 240 c.c.; thin gruel and milk, 90 c.c.
Fourth day	All of gastric aspirations; 6 egg whites; beef juice, 270 c.c.; thin gruel and milk, 1,060 c.c.; liver pulp, 60 Gm. (820 calories).
Fifth day	All of gastric aspirations; 4 whole eggs; 60 Gm. liver pulp; 1 pint milk; 50 Gm. dextrose, cod-liver oil ziii. gruel; beef juice, 240 c.c. (1,790 calories).
Sixth day	All of gastric aspirations; same, but add 100 c.c. orange juice. 25 c.c. karo, and 20 c.c. dilute HCl (1,880 calories).

Tenth day — All of gastric aspirations; beef juice, 240 c.c.; liver pulp, 60 Gm.; 4 eggs; 500 c.c. milk; orange juice, 200 c.c.; dextrose, 50 Gm.; karo, 35 c.c.; cod liver oil, 20 c.c.; dilute HCl, 20 c.c.; 10 per cent Nacl, 50 c.c.; brewer's yeast, 1 dr.; mashed potato, 30 Gm.; purée spinach, 30 Gm.; tomato juice, 50 c.c.; butter, 20 Gm. or cream, 20 per cent, 100 c.c.; gruel, ad lib. (2,200 calories).

He was entirely free of symptoms a year later.

CASE 2.—F. B. (M. G. H. No. 205083) entered the hospital on July 25, 1939, with the diagnosis of obstructing duodenal ulcer. He was a 42-year-old sheet-metal worker, who had had a diagnosis of duodenal ulcer made five years before by x-ray, following a short period of epigastric pain. A month before entering, he began to vomit large amounts of fluid. X-ray studies showed partial obstruction at the pylorus, spasm of the antrum, gastritis, duodenitis, and an active duodenal ulcer. At a repeat examination, after twelve days of medical treatment, no barium could be seen to pass the pylorus during an hour's observation. Accordingly, operation was done. Under spinal anesthesia exploration revealed a very large, indurated mass in the region of the pylorus and antrum, which felt like inflammation rather than neoplasm. A routine posterior gastroenterostomy was done. There were a few adhesions in the region of the ligament of Treitz. A lumen of two or three fingers was obtained.

He immediately began to run a negative gastric balance, which varied from 500 to 1,500 c.c. daily. His blood chemistry showed no remarkable change, and he remained in good condition. On the eighth postoperative day he was again explored. The midline wound was reopened. There was no evidence of peritonitis. Nothing could be felt in the region of the gastroenterostomy to indicate the cause of the obstruction. A loop of jejunum was identified at a point about eight inches from the gastroenterostomy. A No. 16 catheter was inserted and fixed with two purse-string sutures, reinforced by omentum. The catheter was brought out through a stab wound in the left side.

Eleven days after the jejunostomy, he was gotten out of bed. Barium by mouth failed to pass through the anastomosis. Numerous measures were tried to maintain a normal blood chemistry. For several days he received a soft diet by mouth. The gastric contents were aspirated and replaced in the jejunostomy tube. His blood chemistry was kept near normal during the entire period. His urinary output was maintained at about 1,000 c.c. daily. His negative gastric balance was 2,000 to 3,000 c.c. daily. The gastric aspirations were replaced in the jejunostomy tube. He received a total of six transfusions.

On the thirtieth day after posterior gastroenterostomy, and twenty-two days after jejunostomy, he ran a positive balance for the first time. Thereafter, he improved rapidly. Barium by mouth showed an open gastroenterostomy stoma, with narrowing of the efferent loop of jejunum just distal to the stoma. His jejunostomy tube was taken out four days after a positive balance was obtained, and he was discharged from the hospital three days later, on Sept. 15, 1939, on a six-meal bland diet.

A repeat gastrointestinal series, on Feb. 9, 1940, showed barium passed through the gastroenterostomy without delay.

CASE 3.—R. C. (B. M. No. 223829), a 64-year-old native-born policeman, entered the hospital Nov. 7, 1939, complaining of persistent vomiting of five days' duration. He had had symptoms of epigastric distress relieved by soda twenty years before entry. Eleven years ago an x-ray diagnosis of duodenal ulcer was made. Nine years ago and one year ago he had recurrent attacks of pyloric obstruction. He began to vomit three weeks before entry and had been unable to retain any fluids for the past five days.

Physical examination was essentially negative except for obesity and dehydration. The blood count showed 4.29 R.B.C. and a white count of 10,900 with 84 per cent polymorphonuclears. Urine showed a specific gravity of 1.013 with 1 plus albumin. His blood chloride was 77.4 milliequivalents; the N.P.N., 100 mg. per cent; and protein, 7.6 per cent. Gastric analysis showed 48 units of free Hcl and 73 one hour after test meal. A phenolsulphonphthalein test showed about 15 per cent excretion in two hours. Under the fluoroscope, marked pyloric obstruction was observed. No barium passed into the small bowel for two hours. At six hours a small quantity could be seen in the lower jejunum. He was completely obstructed and vomited 58 ounces soon after entry. He was given intravenous fluids and kept on nasal suction for six days. His N.P.N. dropped to 75 during this period. It seemed that no further improvement would occur, so a short-loop posterior gastroenterostomy without clamps was performed. It was noted that the omentum was extremely heavy and the mesocolon quite thick. There was an obstructing duodenal ulcer with marked dilatation of the stomach.

After operation, he ran a negative gastric balance regularly, averaging about 1,000 c.c. daily. He was given quantities of intravenous fluids so that his N.P.N. declined to 50, eight days after operation.

On the ninth postoperative day, because of persistent obstruction, the midline incision was reopened. The stomach had contracted quite remarkably. Two fingers could be passed from above into the anastomosis. No attempt was made to visualize the anastomosis from below, but a loop of jejunum was picked up about twelve inches distal to it. A No. 16 catheter was inserted and brought out in a subcostal position as a jejunostomy. Following the jejunostomy, he was given large amounts of fluid by this route. His N.P.N. continued to rise to 150. Obviously, he was failing to absorb all of the fluid given by jejunostomy. Intravenous saline solution was again employed. On the fifteenth day after jejunostomy, he developed a mild psychosis. During this period he was given chiefly milk, lime water, and vitamins through his jejunostomy. He was transfused a total of five times. On the sixteenth day after jejunostomy (i.e., the twenty-fifth day after posterior gastroenterostomy), his obstruction was relieved. This was proved by the fluoroscope, barium passing readily through the posterior gastroenterostomy.

At the end of this period of obstruction, he was in surprisingly good shape, although his N.P.N. was still 80. A repeat phenolsulphonephthalein test at this time showed less than 15 per cent excretion in two hours. He thereafter ran a positive gastric balance with no more vomiting. He was discharged from the hospital thirty-five days after the original operation.

Six months later the patient reported remarkable improvement. He had been entirely free of gastric symptoms and was working at his regular job.

CASE 4.—F. K. (B. M. No. 271724), a man, 51 years old, entered the hospital on Oct. 14, 1940, with an obstructing duodenal ulcer. He had been vomiting for several weeks and had lost about twenty pounds in weight. Barium studies showed almost complete pyloric retention. A posterior gastroenterostomy was done. He immediately began to run a negative gastric balance, varying from 2,000 to 4,000 c.c. daily. His N.P.N. rose to 50, while his serum protein remained at 6 per cent. Five days after operation, a jejunostomy was performed. Gastric aspirations and added milk and lime water were started almost at once through the jejunostomy tube. On the fourteenth postoperative day, his balance became positive and remained so. Four days later, barium was seen to pass slowly through the anastomosis. He was discharged from the hospital twenty-one days after his posterior gastroenterostomy, having lost very little time from the secondary operation and having gained considerable strength during that period.

CASE 5.—C. H. (B. M. No. 181231), a man, 66 years of age, had a known duodenal ulcer of nine years' duration. For the past six months he had been on a

diet and for one month had had very severe pain. X-ray showed 50 per cent retention in the stomach at the end of six hours and a duodenal ulcer on the posterior superior wall. At operation on Sept. 9, 1940, an active duodenal ulcer was found. A gastric resection was done with an anterior Hofmeister anastomosis. His immediate postoperative course was entirely uneventful. His nasal tube was removed on the fourth day. On the eighth postoperative day, he suddenly vomited 78 ounces. At that time, his N.P.N. was 13 mg. per cent and his protein 6.3 per cent. He then ran a negative gastric balance of approximately 2,000 c.c. daily. Six days afterwards a jejunostomy was done. Thereafter his serum protein remained above 6 per cent until he left the hospital. Fifty days after the resection, his gastric balance finally became positive and he was discharged from the hospital entirely relieved shortly thereafter.

CASE 6.—M. B. (M. G. H. No. 355463), a 24-year-old woman, on Aug. 12, 1936, had a Billroth I resection for a gastric ulcer. Obstruction began immediately after operation. On the fifteenth postoperative day, a jejunostomy was done. The obstruction was relieved on the thirty-second postoperative day and the patient discharged shortly thereafter.

CASE 7.—S. S. (B. M. No. 151669), a 70-year-old woman, had a resection of a carcinoma of the stomach with a posterior Pólya anastomosis on Oct. 3, 1938. There was immediate marked postoperative obstruction. Five days after the resection, a jejunostomy was performed. Thirty-one days after the resection, relief of the obstruction finally occurred. The obstruction in this case appeared to be partially due to an abscess which drained through the lower end of her wound and to a serum protein which remained somewhat low throughout. She was finally discharged in good condition.

CASE 8.—H. B. (B. M. No. 73165), a 50-year-old man, had a Billroth I resection of the stomach for duodenal ulcer on Sept. 2, 1937. There was immediate postoperative obstruction. A week later, a jejunostomy was performed through a left subcostal incision. The anastomosis was found to be entirely normal. He developed wound sepsis, which drained satisfactorily. His obstruction was relieved on the twenty-sixth postoperative day. A year after discharge from the hospital, he had no gastric symptoms.

CASE 9.—S. B. (M. G. H. No. 153343), a 34-year-old man, entered with an obstructing duodenal ulcer. At laparotomy numerous adhesions about the common duct made a posterior gastroenterostomy advisable in preference to a resection. The gastric balance varied considerably from immediately after the operation but averaged about 1,000 c.c. on the negative side daily until thirteen days after operation when a jejunostomy was done. The negative balance then continued undiminished until thirty-one days after operation when the balance became positive and stayed there. The patient's N.P.N. and serum protein remained normal throughout.

CASE 10.—M. D. (B. M. No. 192291), a 74-year-old woman, entered the hospital on May 14, 1939. She had had six weeks of persistent vomiting. At operation, a large carcinoma was found adherent to the pancreas. A posterior gastroenterostomy was done. She began to vomit thick brown fluid almost immediately after operation. She ran a slightly positive gastric balance from the seventh to eleventh days but then it again became negative. Fifteen days after the posterior gastroenterostomy, the upper half of the wound was opened. There were numerous adhesions about the stoma. A Witzel jejunostomy was performed. A negative balance continued postoperatively until twelve days after jejunostomy when she began to take all feedings by mouth for the first time. She improved slowly and was finally discharged.

CASE 11.—J. A. (M. G. H. No. 237423). A gastric resection with a posterior Pólya anastomosis was done on this 65-year-old man on Oct. 25, 1940, for a carcinoma of the stomach. On the following day, he had a negative gastric balance of 1,500 c.c. This amount diminished and there was a slight positive balance from the fifth to tenth postoperative days. It then became negative again. On the fifteenth day a jejunostomy was performed. The gastric balance finally became positive twenty-five days after the resection and remained so thereafter.

CASE 12.—G. L. (M. G. H. No. 164699), a 59-year-old man, had a posterior Pólya resection for carcinoma of the stomach on Dec. 21, 1938. There was immediate postoperative obstruction that persisted until finally on the fifteenth postoperative day, a short incision was made under novocain beneath the left costal margin. A deliberate exploration was avoided. There were many adhesions observed about the anastomosis. The upper portion of normal bowel that was observed was used as a jejunostomy. Three days after this operation, it was noticed that jejunostomy feedings were immediately returned from the nasal tube. Dye introduced in the jejunostomy tube also appeared in the same way. The patient's N.P.N. remained at a normal level and his serum protein was 6.6 and 5.7 per cent at two determinations. He gradually lost ground and died on the twenty-ninth day after resection of bronchopneumonia. When jejunostomy was performed on this patient, it was done at too late a date and also was not done in the proper technical manner. This patient probably had definite stomal obstruction that persisted until practically no peristaltic activity was left in the small bowel. On the other hand, he may have had high jejunal obstruction from the beginning that was not discovered at the time of the exploration.

CASE 13.—W. I. (M. G. H. No. 163447), a 70-year-old man, was admitted to the hospital with carcinoma of the stomach and had a posterior Pólya anastomosis following a gastric resection on Dec. 14, 1938. There was a freely movable tumor and no evidence of metastatic disease. He ran a slight negative balance for four days and then this progressively increased until he was losing nearly 1,500 c.c. more by nasal tube than he was taking by mouth. Sixteen days after the first operation, a jejunostomy was done. The old incision was opened, many adhesions were found, and a Witzel type of jejunostomy was performed. His N.P.N. remained at a normal level. His protein was 5.5 and 6.4 per cent at two determinations. He lost ground steadily following his original operation and died two days after the jejunostomy. The cause of death as determined at autopsy was bilateral bronchopneumonia and pulmonary infarction. This was a patient of the older age group, who should have had a jejunostomy much earlier.

CASE 14.—C. C. (M. G. H. No. 16619), a 60-year-old man, had a posterior gastroenterostomy done for an obstructing duodenal ulcer on March 8, 1938. The transverse mesocolon was short and the procedure difficult. His preoperative N.P.N. was 87 and 117, while the serum protein was 5.2 per cent. He immediately began to run a large negative balance. However, with intravenous fluids, his N.P.N. came down to 32 and 35 mg. per cent and his protein rose to 6.4 and 6.7 per cent. He was finally explored because of persistent obstruction thirteen days after the original operation. Several adhesions were found about the distal loop and it was believed that they accounted for his obstruction; they were accordingly mobilized. No further procedure was done. He failed to improve so four days thereafter a jejunostomy was finally performed. He had been going steadily downhill and died three days after the jejunostomy with an N.P.N. of 102. Autopsy revealed no significant cause of death. This patient was uremic with a high N.P.N. before operation. His serious condition was not appreciated. Exploration was done too late on the thirteenth day and obviously should have included jejunostomy.

CASE 15.—J. L. (M. G. H. No. 29978), 60 years of age, was admitted for an obstructing duodenal ulcer and had a posterior gastroenterostomy performed on March 18, 1937. The operation was extremely difficult on account of a good deal of fat in the transverse mesocolon. He began to obstruct on the sixth postoperative day. He also developed a septic wound and partial wound separation. Finally after the obstruction failed to subside, twelve days after the original operation, he was again explored. There were numerous adhesions of the small bowel, especially about the stoma. An anterior gastroenterostomy was performed. This failed to function at all. After six days, another exploration was carried out. Numerous adhesions again were found. A tube was put in the upper jejunum. It was then found that fluid put in this jejunostomy tube came back through the stomach. Nine days after the original operation, another lower jejunostomy was made. This contributed nothing and the patient died two days later. The cause of death was plastic peritonitis. This was an old patient whose obstruction was complicated by other factors, such as a plastic peritonitis and wound separation. The obstruction was apparently not merely at the stoma but also at several other points in the jejunum.

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SECTION OF THE SPINOTHALAMIC TRACT IN THE MEDULLA WITH OBSERVATIONS ON THE PATHWAY FOR PAIN*

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SINCE Spiller (1905) first concluded that the pathway transmitting pain and temperature sensations resides in the anterolateral columns, knowledge concerning the spinothalamic tract has advanced considerably. The observations of Collier and Buzzard (1903) upon the course of the tract through the cord to the ventral nucleus of the thalamus were elaborated in greater detail by Goldstein (1910). More recently Foerster and Gagel (1931) and Walker (1940) have traced the spinothalamic tract in Marchi preparations following anterolateral chordotomy.

A topical arrangement of fibers within the cord was suggested, among others, by Foerster and Gagel (1931), the fibers from the upper segments of the body lying more centrally and fibers from the lower segments occupying a more peripheral position in the spinothalamic tract. With minor modifications this arrangement has also been noted by Hyndman and van Epps (1939) and by Walker (1940). On the basis of animal experiments (LeGros Clark [1936], Walker [1938]) topical localization of fibers from various segments of the body has been demonstrated within the thalamus, and it is probable that a regular arrangement of fibers is present in the brain stem.

In the brain stem the spinothalamic tract is relatively superficial on the dorsolateral surface of the inferior olive. It then courses more deeply until the anterior border of the brachium pontis is reached; at this point it turns dorsally to occupy a superficial position once more. Dogliotti (1937, 1938) has reported cauterization of the tract in the mesencephalon by a supratentorial approach, resulting in analgesia of the contralateral half of the body. He has made no reference to the question of topical localization.

Recently one of us (H. G. S.) sectioned the spinothalamic tract at the junction of the middle and lower thirds of the inferior olive for relief of intractable pain. Prior to operation, careful examination revealed no diminution in or loss of any sensory modality. Sensory changes which occurred in different parts of the body during the operation were correlated with increasing depth of incision. In addition, observations upon partial section of the descending spinal tract of the trigeminal nerve were made.

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CASE REPORT.—The patient, a 30-year-old white woman, was referred to the neurosurgical service of the St. Louis City Hospital for relief of pain. Four years previously she first noticed a painful swelling of the left jaw. For two years she sought relief by morphine. In October, 1938, a mixed tumor was removed from the left submaxillary region. In April, 1939, a recurrence was apparent; the patient again resorted to morphine. She began to complain of pain in the chest; x-rays showed invasion of the left lung. There were several subsequent admissions until the end of May, 1939, when she was brought to the hospital after attempting suicide. On the advice of the neuropsychiatrists she was allowed to remain in the hospital to prevent self-destruction.

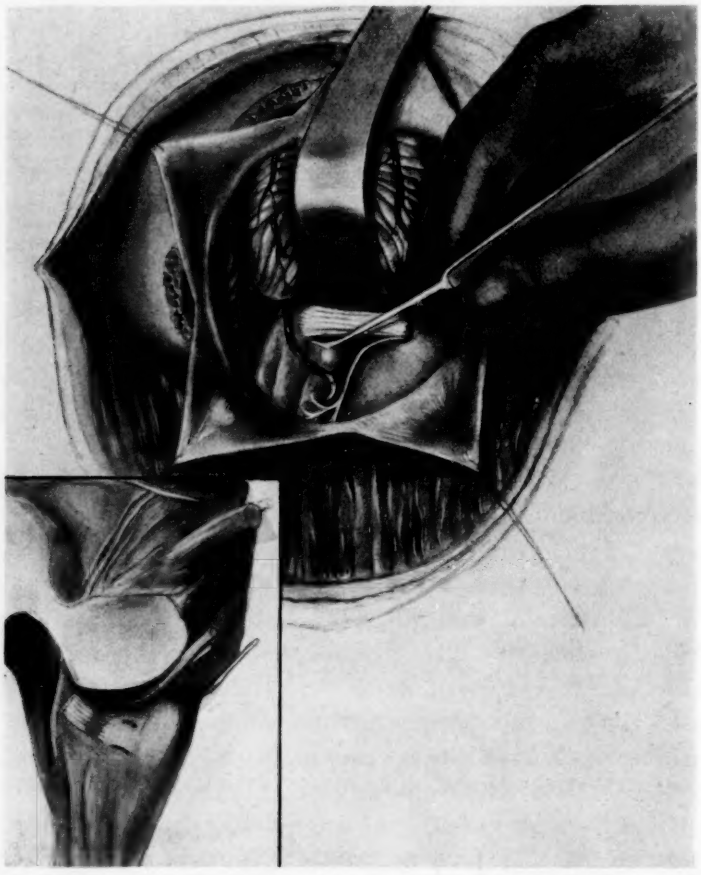
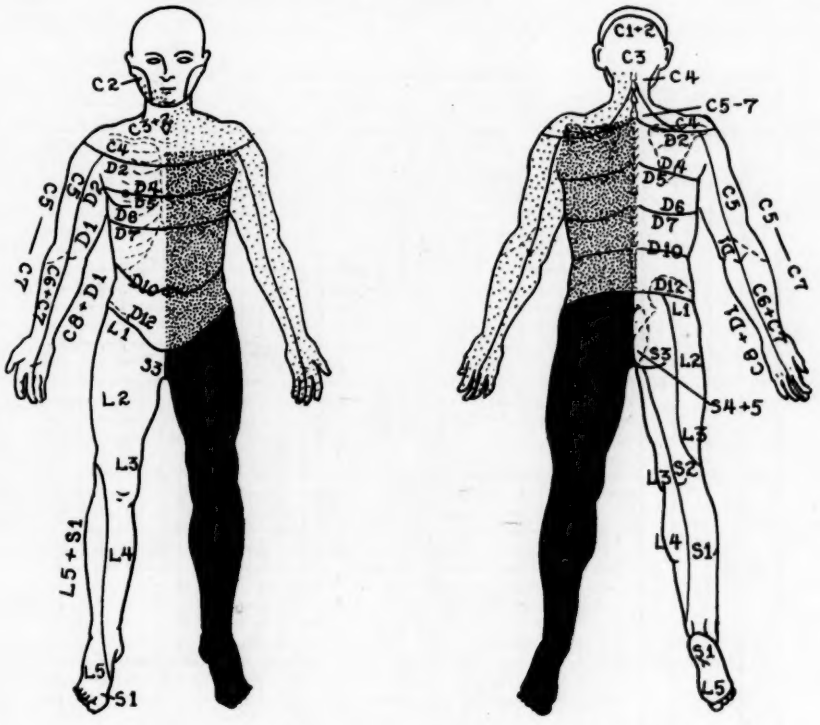


Fig. 1.—Showing exposure of right lateral wall of medulla for section of the spinothalamic tract. Knife point is directed between the roots of the vagus and the caudal portion of the inferior olive. Posterior inferior cerebellar artery is shown in its retracted position. Inset figure shows operative relations from a lateral view of a dissected brain stem, with the roots of the ninth and tenth nerves reflected back. The more rostral curved line indicates the site of incision which interrupted the descending trigeminal tract. The caudal line represents the point of entry of the incisions into the spinothalamic tract.

Pain in the left side of the neck, chest, and abdomen became worse, overshadowing the original mandibular pain. Steadily increasing doses of morphine were inadequate. There was no pain on the right side. In view of the distribution of the pain it was questionable whether even a high cervical section would be effective; in addition, since the left lung field was already practically functionless, the danger of traumatizing the fibers of the right phrenic had to be considered.

The possibilities for relief of pain and the danger of section of the spinothalamic tract at the level of the olive were fully explained to the patient. Despite the hazard involved, she begged for the operation. While waiting for the patient's scattered relatives to be found, her pain became progressively worse, until she was receiving 11 gr. of morphine daily with no more than transitory relief.

Operation.—(Jan. 27, 1940.) Avertin plus 3 gr. of morphine had no effect upon the patient's state of consciousness. Since we could rely upon her cooperation, it was decided to go ahead with local anesthesia. This made it possible to determine the effect of section during the operation.



Complete analgesia and loss of "tickling" sensation. Blunt touch preserved.

Almost complete analgesia and loss of "tickling" sensation.

Hypalgesia and diminished "tickling."

Fig. 2.—Illustrates the results of the postoperative sensory examination which was checked repeatedly.

A suboccipital skin incision was made (Fig. 1). The occipital bone was removed on the right side to just beyond the midline. After opening the dura and evacuating the spinal fluid in the cisterna magna, the right cerebellar tonsil was retracted upward. The right lateral wall of the medulla was exposed. The cervical roots of the spinal accessory nerve were identified, and then in succession the posterior inferior cerebellar artery, the bulbar portion of the spinal accessory,

the roots of the vagus, a small vein, and the glossopharyngeal nerve were encountered. The rostral part of the inferior olivary eminence was visualized just in front of and ventral to the ninth nerve. At this site, an incision about 3 mm. deep was made just ventral to the point of emergence of the glossopharyngeal nerve and paralleling its intrabulbar course. The patient complained of excruciating, lightning-like pain in the right jaw at the moment of incision. Examination showed no change in sensation over the body. From this, it was obvious that the descending trigeminal tract had been partially interrupted, and that the spinothalamic tract was not in the line of incision. Accordingly, the caudal portion of the inferior olive was exposed by gentle displacement of the posterior inferior cerebellar artery. An incision about 3 mm. in depth was then made

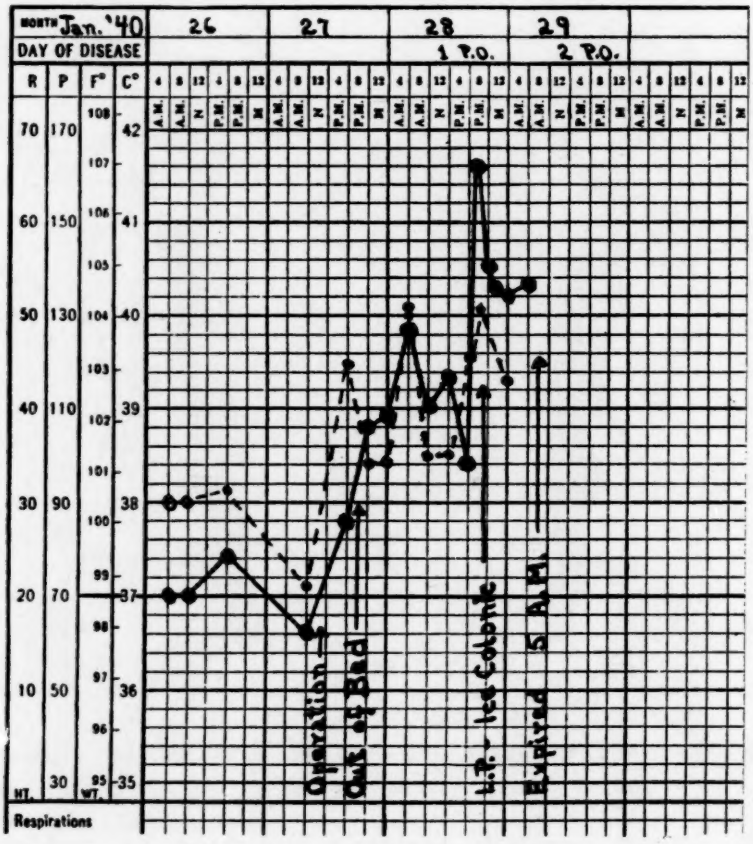


Fig. 3.—Chart representing the postoperative course.

between the undersurface of the vagus rootlets and the olive, these two structures serving as excellent landmarks. Examination showed loss of sensation to pinprick in the entire left lower extremity. In order to abolish pain completely a second incision was made at this same level, extending more medially to a depth of about 6 mm. It was designed to skirt the dorsal margin of the olive and so interrupt the remaining spinothalamic fibers which lie in this position (Goldstein [1910]). As this incision was progressively deepened, there resulted a corresponding progressive diminution of pain sensibility over the left side of the abdomen, chest, and upper extremity. The patient volunteered the information that the severe pain of the abdomen, chest, and neck was entirely gone. The only pain that persisted was confined to the left mandible. Trigeminal tractotomy

on the left side (by Sjöqvist's method [1938]) could have been performed through the same exposure. However, this was not thought justifiable since the residual pain was not very severe and could probably be relieved by alcohol injection of the third division later. The wound was closed in layers with silk. There was no respiratory embarrassment or difficulty in swallowing. The patient was sent back to the ward, grateful for relief of pain.

Course.—Fig. 2 shows the results of postoperative sensory examination which was checked repeatedly. There was complete analgesia and loss of "tickling" sensation over the entire lower extremity, with preservation of touch. There was almost complete analgesia over the trunk to the level of the clavicle. There was hypalgesia over the arm and neck up to the left mandible. In addition there was hypalgesia over the right mandible in an area corresponding to the distribution of the third division of the trigeminal nerve. The patient was completely free of pain except for the area of the left jaw. There was no motor weakness or ataxia. Sweating was equal on the two sides.

Fig. 3 represents the postoperative course. The patient's condition was excellent throughout the first day. At 7:00 P.M. on the evening after operation, she left her bed unassisted to look for a cigarette. The patient was rational and showed no apparent ill effects when she was visited at midnight. The next morning, temperature reached a peak of 103.8° F., but fell slowly to 101.2°, at 4:00 P.M. Her condition seemed to be excellent. Then there was a sudden spike to 107° with delirium. Lumber puncture was done; the fluid contained no more blood than is usually found after a craniotomy. Efforts to reduce the fever were only partially successful and the patient died two days after operation.

Autopsy.—A post-mortem examination was performed three hours after death by Dr. George Fraser of the Department of Pathology, St. Louis City Hospital. There was recurrence of mixed tumor in the submaxillary region. The left lung was almost solid with tumor; the right lung partly so. There was extensive metastatic involvement of the pleura, aortic nodes, diaphragm, liver, and the left kidney.

Examination of the Brain (J. L. O'L.).—There was no gross abnormality. The operative site was clean; there was no evidence of hemorrhage or edema. The sites of entry of the incisions were apparent. Thin slices made through the hemispheres, thalamus and hypothalamus showed no evidence of tumor invasion. The brain stem and attached remnants of the cerebellum were fixed in 15 per cent formalin. Later it was divided into blocks of convenient size, embedded in celloidin, and sectioned serially in a transverse plane at 40 microns. The sections were stained by the Kulschitzky modification of the Weigert method.

Microscopic Examination.—Serial Weigert sections of the brain stem from the level of the nucleus ruber to the rostral pole of the eighth nerve entry zone showed no evidence of secondary involvement of local lesions. In particular the fiber bundles of the lemniscus systems stained normally and equally on the two sides.

1. *Right Trigeminal Tract Lesion:* Just rostral to the known intramedullary course of the ninth nerve, an elongated lesion was observed in the dorsolateral area of the medulla. This lesion entered at the ventromedial angle of the restiform body and passed dorsally and somewhat medially to interrupt the ventrolateral part of the spinal trigeminal tract. At the point of entry the lesion was somewhat caudad to the cochlear division of the eighth nerve. It partially destroyed the spinal trigeminal tract at the level of the dorsal cochlear nucleus. (Figs. 4*A* and *B*.) The lesion was 3 mm. deep and extended over 56 40 micron sections (2.2 mm.). The lesion was too far lateral to interrupt the probable course of the spinothalamic tract at this level. It is possible that the olivocerebellar system was moderately damaged and that some secondary cochlear fibers directed toward the trapezoid decussation were interrupted, but no evidence of such involvement was apparent postoperatively.

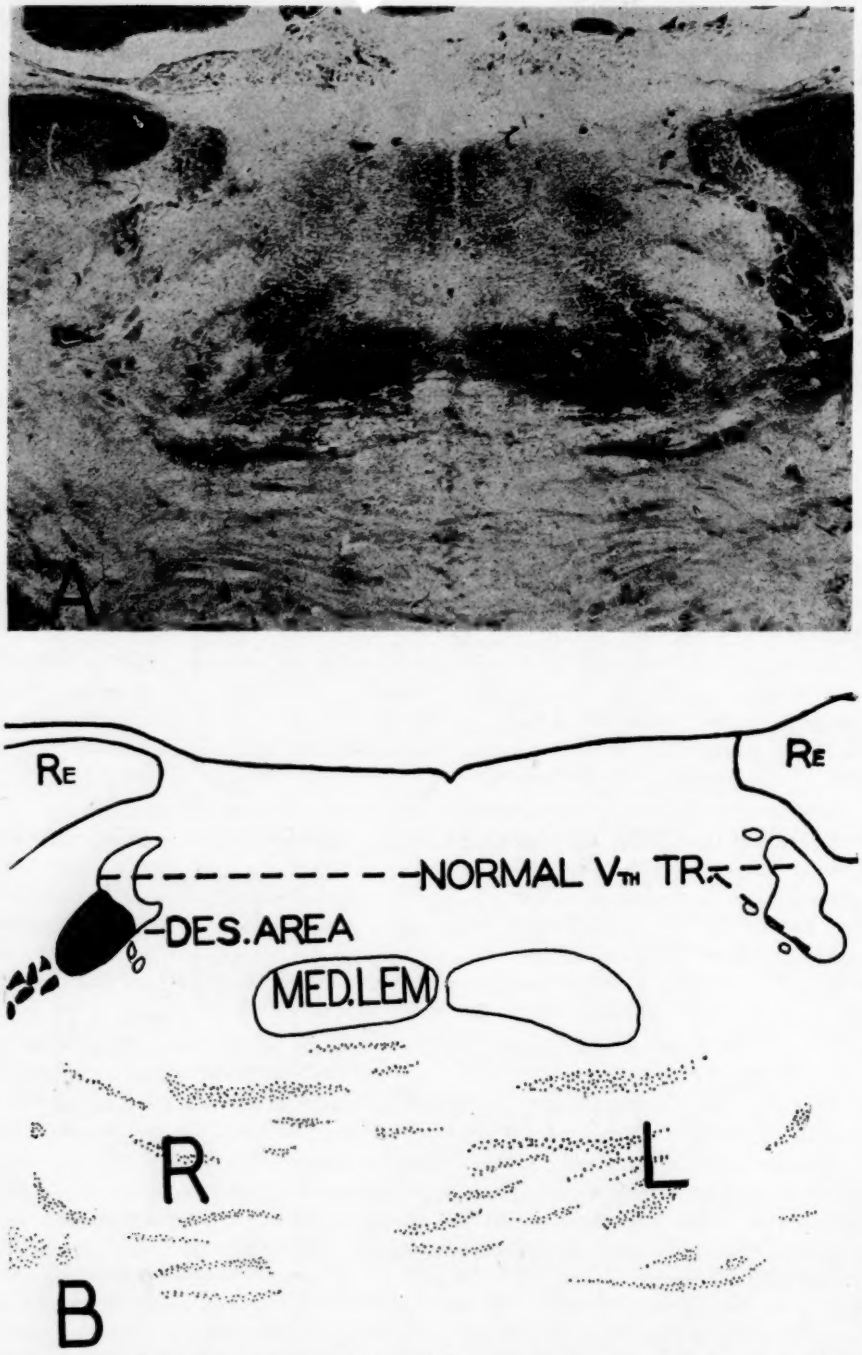


Fig. 4.—*A*, Photograph of a 40 micron transverse section through the medulla. The figure appears transposed when compared with Figs. 5*A*, *B*, *C*; this resulted from mounting sections from adjoining blocks in reverse order. *B*, Corresponding outline sketch: *R*, right; *L*, left; *Re*, restiform body; *med. lem.* medial lemniscus; *des. area* (solid black), interrupted fibers of right descending trigeminal tract, 5.5. diameters.

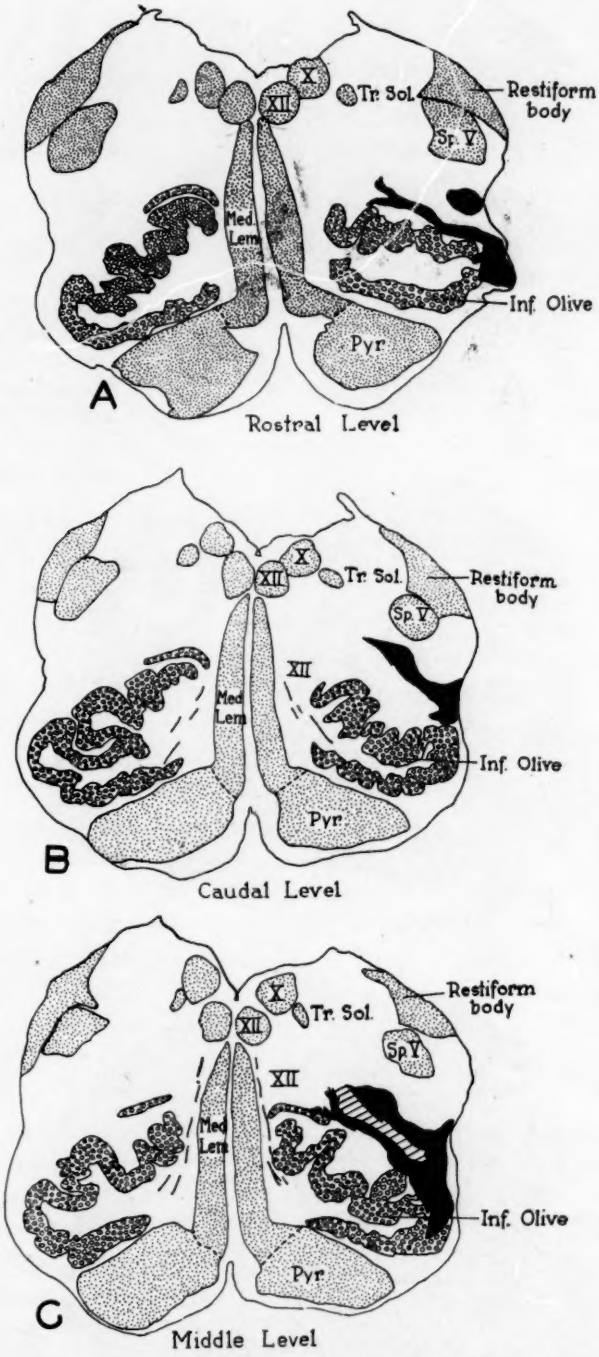


Fig. 5*A*, *B*, and *C*.—Outline drawings of transverse levels of the inferior olive, illustrating the situation and extent of the rostral (*A*) and caudal (*B*) lesions placed in the right spinothalamic tract. In *C* the total lesion is reconstructed upon a transverse section midway between *A* and *B*. *XII*, hypoglossal nucleus; *X*, dorsal motor nucleus of the vagus. *Tr. Sol.*, tractus solitarius; *Sp. V*, descending trigeminal tract.

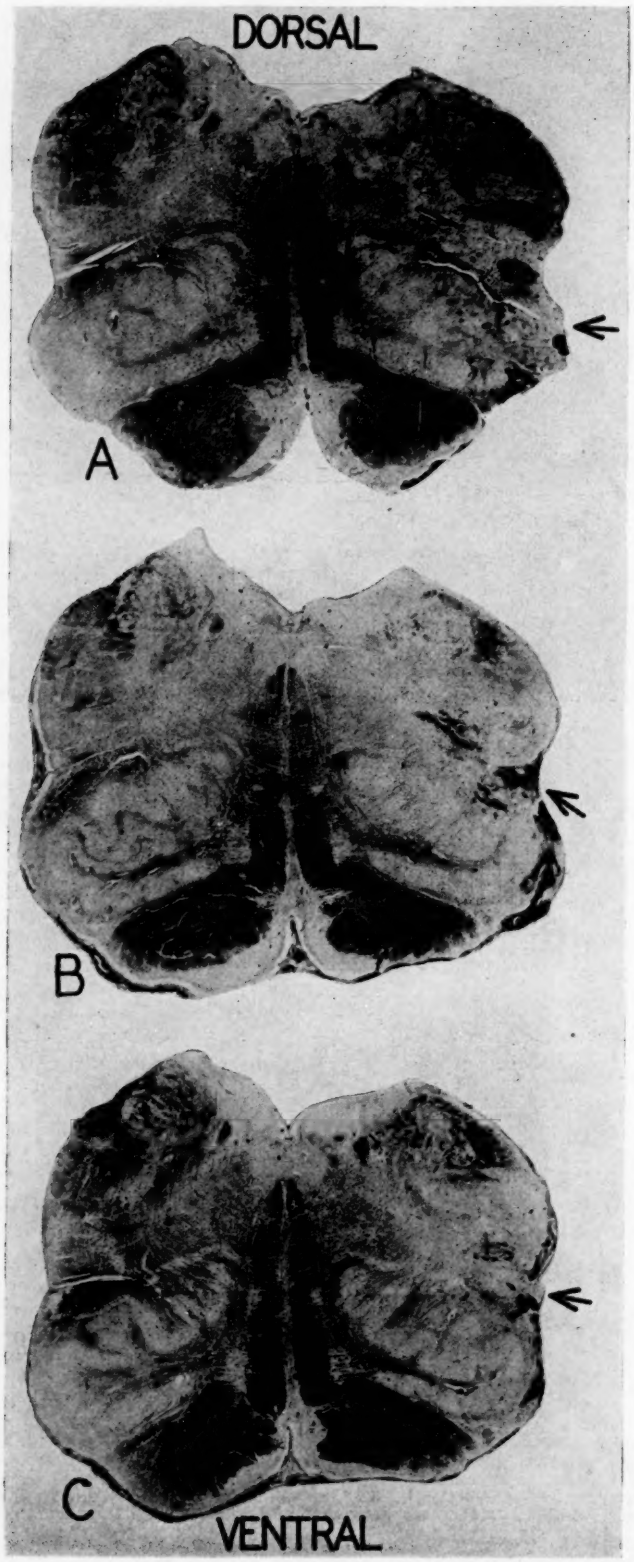


Fig. 6*A*, *B*, and *C*.—Photographs of transverse levels of the medulla corresponding to the outline drawings in Figs. 5, A, B, and C. Arrows indicate situation of lesion, 3.5 diameters.

2. *Right Spinothalamic Tract Lesion:* Situated in the posterolateral sulcus overlying the lower third of the inferior olivary nucleus, a superficial lesion was detected. From this point of entry two stabs extended into the lateral area of the medulla, between the dorsolateral surface of the inferior olive and the ventrocaudal margin of the restiform body. The deeper and more rostrally situated of these stabs (Figs. 5*A* and 6*A*) shows a narrow tract which follows the dorsal margin of the inferior olivary nucleus. This lesion was 5.5 mm. deep and in its medial extent was separated by 3 mm. from the lateral margin of the medial lemniscus and by 4.4 mm. from the median raphe. Similar distances separated it from the dorsal motor nucleus of the vagus and the tractus solitarius.

The more caudal stab (Figs. 5*B* and 6*B*) was 4.3 mm. deep and was more dorsally situated, coursing just ventral to the spinal trigeminal tract but apparently not interrupting any of its fibers. Likewise its tip was well separated from the dorsal motor nucleus of the vagus and tractus solitarius.

The rostrocaudal extent of the entire spinothalamic tract lesion was confined to 45 40 micron sections (1.8 mm.). Fig. 5*C* reconstructs upon an outline drawing the whole area interrupted by the incision. Except for a focal softening upon the superolateral margin of the inferior olive there was a minimum of tissue damage at the margins of the lesion.

COMMENT

The observations on the sensory loss in this case may be considered in relation to the spinal trigeminal tract first and then the spinothalamic tract.

Davis and Haven (1933) have made careful observations on the deficit following experimental section of the sensory root of the trigeminal nerve in cats. Their experiments were microscopically controlled. They concluded that the posteroinferior portion of the root at its entrance into the pons carries the fibers of the ophthalmic division; in the spinal tract itself they found this arrangement is preserved so that the ophthalmic fibers lie in the ventral portion and the mandibular fibers lie in the dorsal portion. In man Sjöqvist (1938) has studied one patient who died several years after a differential section had been performed through the suboccipital approach. In this case the posterior inferior two-thirds of the root had been cut. No loss of sensation could be observed but the patient was free of second division pain for three years. In Kulschitzky sections Sjöqvist found degeneration in the dorsal part of the spinal trigeminal tract. He concluded that "the portion of the root which is cut at the Dandy operation corresponds to the dorsal (or superior) part of the tract and nucleus. This portion consequently must be formed by maxillomandibular fibers."

In the case that is presented in this paper there is evidence that the mandibular fibers of the trigeminal nerve were injured. At the moment of incision the patient complained of severe pain in the right (ipsilateral) jaw. Subsequent examinations demonstrated diminished pain sense in the distribution of the third division. Histologically, the lesion involved the ventrolateral portion of the spinal trigeminal tract. In this case, therefore, it appears that at the level of the dorsal cochlear nucleus the mandibular fibers are represented in the ventral rather than the dorsal area of the descending tract.

It is noteworthy that, although the patient complained of pain when the descending trigeminal tract was cut, there was no complaint when incisions were made into the spinothalamic tract. The explanation for this probably lies in the fact that in the former instance primary pathways were injured, while in the latter case secondary fibers were cut.

With regard to topical localization in the spinothalamic tract, the observations support the premise that in the brain stem, as in the cord, the fibers from the lower segments lie dorsolaterally, while those from the upper segments have a more ventromedial position. It was clear from examination made during the operation that the lower segments were affected by the dorsal incision into the tract and the upper segments were not involved until the second (ventral and medial) incision was made.

The association of loss of "tickling" sensation with loss of pain supports the view of Zotterman (1939) that these modalities are mediated by small fibers (less than 10 microns) which make up about 98 per cent of the fibers of the spinothalamic tract (Häggqvist [1936]). The observations in the present case offer no additional evidence concerning the position of the secondary tactile fibers in the brain stem.

SUMMARY

A case is reported in which section of the spinothalamic tract in the medulla was performed for relief of high, intractable pain. The operative technique is described. On the basis of sensory changes which resulted, it is concluded that a topical arrangement of fibers is present in the spinothalamic tract, with fibers from the lower dermatomes occupying a dorsolateral position and those from the upper segments lying ventromedially. A lesion involving the ventrolateral portion of the descending trigeminal tract was associated with disturbance of sensation in the distribution of the mandibular division of the fifth nerve.

Since this report was accepted for publication, Dr. James C. White (personal communication), of Boston, has confirmed the efficacy of the procedure, successfully relieving pain in a patient suffering from Raynaud's disease.

We have had additional experience in a second case of advanced malignant disease, in which the left spinothalamic tract was cut at the level of the inferior olive. This resulted in complete alleviation of pain in the right chest, shoulder, and axilla, caused by inoperable carcinoma of the breast with metastases. There was no involvement, indicating that the lesion extended into the neighboring descending tract of the trigeminal nerve, the nucleus ambiguus, medial lemniscus or vagal autonomic centers. We were able to confirm our previous opinion concerning topical localization of pain fibers within the spinothalamic tract in the brain stem. The patient was discharged from the Neurosurgical Service of the St. Louis City Hospital and was free of pain until her

death from carcinoma one month later. Details of this case will be reported in a subsequent communication.

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WOUND HEALING

With Especial Reference to Muscle and Fascia Repair

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IT IS most generally held that, when muscle is severed and sutured, healing occurs by means of fibrous tissue elements from the epi-, peri-, and endomysium. Certain recent experimental studies on muscle repair indicate that muscle cells may regenerate (Forbus, 1926; Millar, 1934; Speidel, 1938; and Tauchi, 1934).

In 1923 Seelig and Chouké found that the suture of muscle to fascia failed to establish a firm union. Fascia sutured to fascia, on the other hand, united firmly. In the experiments here reported we have studied the healing of muscle and of fascia following incision such as surgical expediency would require. No attempt has been made to alter the physiology of the parts. The possible influence of various suture materials was also noted.

METHODS

Seventy-two experiments were performed, sixty on twenty-one dogs and twelve on twelve rats. Thirty-three of the experiments on dogs involved suturing of muscle to muscle. All the experiments on rats concerned muscle-to-muscle union. In twenty-five experiments on dogs fascia was sutured to fascia. In two experiments the muscle-to-fascia union was restudied. Various muscles were employed in these experiments, such as the pectoralis major, external oblique, rectus abdominis, latissimus dorsi, trapezius, and others. The usual aseptic surgical technique was employed in the experiments on dogs but in the rats no special precautions were taken. Under anesthesia a particular muscle or fascia was exposed and freed of superficial areolar tissue. In most of the experiments the sutures were placed before the muscle was cut. Suturing was at right angles to the incisions. An attempt was made to secure close approximation of muscle edges without causing tension. The usual cut was transverse; in a few animals, however, oblique or longitudinal incisions were used. Since Howes (1933) reported that healing in some tissues seemed to be influenced by the variety of suture material, we used several different kinds, various sizes of black silk and plain and chromic catgut. After suturing the muscle, the overlying tissue and skin were closed, the latter by means of a subcuticular stitch. The wound was then sealed with collodion.

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The animals were sacrificed at from 8 to 142 days and a large piece of muscle or fascia containing the operated tissue was removed. The tissue was fixed in a modified Kaiserling solution and was later sectioned and examined microscopically for healing and type of union. Two animals showing slight wound infections were excluded from the series.

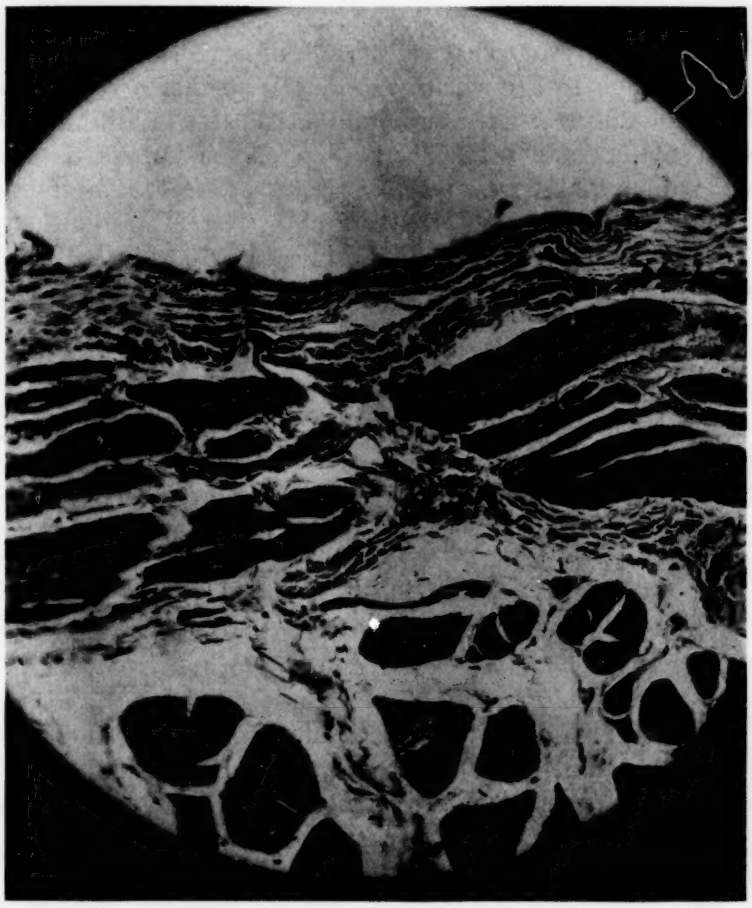

Fig. 1.—Showing area of union of severed striated muscle (×130). Muscle from right back region, eighty-four days after operation.

RESULTS AND DISCUSSION

In the dog the skin wounds were almost healed eight days after suture; the union of muscle to muscle and of fascia to fascia was slightly less firm. Good healing occurred in muscle and in fascia in eleven days. Complete repair seemed to be present after sixteen days.

Microscopic study showed the healing to be the result of connective tissue growth and not through muscle cell regeneration (Fig. 1). We saw no evidence of typical or atypical muscle cell division in these experiments.

According to the experiments of Seelig and Chouké (1923) on dogs, normal muscle did not establish a firm union with fascia but fascia united readily with fascia. Koontz (1926) differed with these results. He believed that the union between muscle and fascia which he obtained was due to the removal of intervening areolar tissue. Hertzler (1927), commenting on this controversy, states: "Fibrous tissue alone can form a union. Fat bearing tissue prevents healing because fibrin bundles cannot form in the presence of fat. Muscle fibers will not heal; it is only the perimysium that can form a union. The ligature must be tied tight enough to traumatize the muscle so that a reaction is produced. It is this traumatic reaction which sets in action the fibrin formation that results in the formation of the fibrous tissue which makes the union." Hertzler believed that the different results reported by Seelig and Chouké and by Koontz could be explained on the ground that loose sutures were used by the former and tight sutures which traumatized the muscle were used by the latter. Seelig and Chouké felt that Koontz's own data showed that union between muscle and fascia occurs only between fascia and the fibrous elements of muscle.

According to MacCallum (1898), the muscle cells multiply and increase in bulk until the embryo is between 130 mm. and 170 mm. crown-rump length. After this stage, he writes: "The fibres now grow in length and thickness, but probably no longer increase in number. In embryos smaller than 170 mm. in length there is a regular increase in the number of fibres found in a cross-section. After this, however, the number remains approximately constant." As in normal growth, our experiments did not show the formation of any new muscle cells. The repair took place by means of the fibrous connective tissue formed between the cut ends of the muscle fibers. Recently both preserved and living fascia lata has been used in the repair of hernias (Haas, 1931; and Hodgkins, 1930). According to Haas (1931), the union affected by these depends mainly on ingrowth of endo- and perimysium: "The muscle cells themselves appeared to be transformed into elements of fibrous tissue."

Our findings differ from those of Forbus (1926) in rabbits and from those of Speidel (1938) in tadpoles. The differences may be attributed in part to the techniques employed. In our experiments the muscle fibers were severed; in those of Forbus the muscle was injured by injection into it of irritant substances. This damaged the muscle fiber, but its sarcolemma remained intact. Speidel observed complete regeneration of the muscles of the tadpole's tail after various kinds of injuries. He mentions cutting and bruising but omits the details concerning regeneration after these procedures. Further Speidel studied larval amphibian forms while our work is based on incisional trauma in adult mammals.

Correlating our results with those of Seelig and Chouké (1923), the union between muscle and muscle and between fascia and fascia is

much firmer than the union between muscle and fascia. The union between muscle and fascia, even after complete removal of areolar tissue from both, was no more firm than that found by Seelig and Chouké.

In our experiments the kind of suture material employed did not appear to influence the nature or degree of union in either muscle or fascia.

SUMMARY

1. Healing of severed, striated muscle of dogs and rats occurs by fibrous connective tissue growth from the epi-, peri-, and endomysium, and not through regeneration of muscle cells.

2. Fascia unites readily to fascia, when closely approximated, by connective tissue growth.

3. The type of suture material employed (silk or catgut) did not appear to influence the degree or extent of union between fascia or muscle.

4. A firmer union developed between muscle and muscle and between fascia and fascia than Seelig and Chouké observed between muscle and fascia.

5. The union of muscle to muscle and fascia to fascia is complete eight to eleven days after suture.

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THE MANAGEMENT OF POSTOPERATIVE WOUND SEPARATION

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ONE of the most serious complications of laparotomy is the breaking open of the wound. The occurrence of this condition fortunately is low, for, even if allowance is made for unrecorded cases, published statistics indicate that approximately only 1 per cent of abdominal wounds disrupt. But if the frequency is low, the mortality is high, varying, according to the literature,[1, 4] from 25 to 50 per cent. Perhaps a 35 per cent mortality is a fair estimate. While it must be admitted that the cause of death in many instances is due to underlying pathologic conditions, at the same time, the method of management currently in vogue deserves attention.

GENERAL MEASURES

Regardless of the course of treatment about to be pursued, the first requisite is to allay the patient's fear by administration of barbiturates. Seconal gr. 1½ to gr. 3 by mouth, if it can be retained, or sodium phenobarbital gr. 1½ by hypodermic, if there is nausea, removes apprehension. There is seldom a complaint of pain in the presence of wound disruption. On the contrary, many patients admit to relief of distress when the wound margins separate. However, morphine sulfate, gr. ¼, by hypodermic should be given to prepare the patient for a general anesthetic, to augment local anesthetic, or to relieve the distress of manipulation when nonoperative procedures are employed.

The next most important step in treatment is to arrange for a blood transfusion as soon as possible, for it should not be overlooked that these patients are seriously ill. Apart from the correction of hypoproteinemia,[8] if this condition exists, blood is the best supportive and restorative medium at the surgeon's disposal. It is also essential to control vomiting, when present, by means of the indwelling duodenal tube, and to restore the fluid level, when indicated, by the intravenous administration of 5 per cent glucose.

IMMEDIATE SUTURE

The teaching and practice of most surgical centers is to advise immediate resuture of the wound when disruption occurs. In most instances, closure of the wound is accomplished by through-and-through suture of silver wire,[6, 7] steel wire, silkworm gut, or braided silk. Layer suture is seldom possible, because the usual finding is that the layers of the abdominal wall are so well agglutinated that they cannot be separated

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into component parts. This agglutination has led observers to consider the possibility that postoperative wound separation in the absence of frank infection is due to catgut allergy. Some support is lent to this hypothesis by consideration of the source of the blood-tinged fluid that stains the dressing before separation actually occurs. Edema of the tissues plus excessive fluid formation indicates that the inflammatory reaction incidental to healing has exceeded normal bounds and, in this respect, simulates an allergic reaction. The chief advantages of suture are that complete replacement of prolapsed intestines is effected without delay and that, in lesser degrees of separation, suture will prevent extension of the process and further eventration. Other advantages are that the period of hospitalization is less and that there is more likelihood of healing without hernia formation than when nonoperative treatment has been employed. The chief disadvantage of suturing is that the procedure subjects an already sick patient to an operation of some magnitude. Certainly only relatively few patients whose laparotomy wounds break open are in condition to stand the shock of a general anesthetic and even a minimal operative procedure. Each patient will stand just so much operative trauma, and disaster is certain to follow when this limit is exceeded. A study of the mortality rate following secondary closure in wound disruption indicates that this threshold has been overstepped on many occasions. Patients who would not be considered good risks for the second stage of a divided operation are subjected to secondary closure, simply because an emergency exists. Immediate operation has long been demanded for surgical emergencies, but gradually the concept has arisen that preparation of the patient for operation is of equal, if not greater, importance than the operation itself. Thus no longer is the dehydrated, shocked, or anemic patient submitted to operation, but rather surgery is deferred until blood and fluid levels are restored. But if this is true of most present-day surgical emergencies, it does not hold for the serious emergency of wound disruption, for most patients with this complication are submitted to operation without delay. In consideration of the course of action to be followed in any surgical emergency, it is well to bear in mind that the decision not to operate is just as important as the decision to operate. The former, however, requires more fortitude on the part of the surgeon, for, while all observers consider themselves capable of passing judgment on occasions when failure to operate might have been the cause of a fatality, few give any consideration to the role played by untimely operations.

Immediate suture of wound disruption should be carried out only in the best-risk patients. If there is any question regarding the ability of the patient to stand the operation, nonoperative methods of treatment are clearly indicated. It is questionable if inhalation anesthetics should ever be administered to these patients, because the straining so often

associated with induction is likely to increase the amount of separation and prolapse. Furthermore, since coughing is the chief predisposing factor in wound separation, an anesthetic agent which is not irritating to the respiratory system should be chosen. Spinal anesthesia fulfills the requirement, but increasing experience has taught that spinal is not the anesthetic of choice for poor-risk patients. These objections, then, limit the selection to local anesthesia. Subcostal block plus infiltration of the wound margin and extraperitoneal tissues with 0.5 per cent novocain solution skillfully and patiently administered will permit reduction of the prolapse and suture of the wound margins without undue discomfort to the patient. Preliminary medication with seconal gr. III by mouth and morphia gr. ¼ by hypodermic will diminish both the psychic and actual distress of the patient. If it is not feasible to move the patient to the operating room in his bed, he should be operated upon in his room. The practice of lifting patients out of their beds onto a stretcher, taking them to the operating room, and then transferring them to an operating table is to be deplored, because these movements, no matter how carefully controlled, increase the amount of prolapse and add to the shock of an already sick patient. Layer suture is rarely possible because of edema and agglutination of the tissues. In the vast majority of cases, closure is best effected by through-and-through sutures. These are put in at intervals of 3 cm. and should be placed about 5 cm. from the wound margins. Care should be exercised when closing an infraumbilical incision not to include the deep epigastric artery in the bite of the suture, lest the vessel be eroded from pressure of the suture material and serious hemorrhage ensue. Silver wire still holds the field as the choice of suture material, although it is possible that the newer plastic suture materials may in time supplant it. The great advantage over silkworm gut is that wire does not tend to cut through the tissues because of its larger diameter. Braided silk is flexible and easier to handle, but stitch abscesses almost invariably form around the skin openings.

CLOSURE BY ADHESIVE STRAPPING

Adequate sedation, using opium derivatives and barbiturates, is the first requisite. Absolute asepsis is maintained only when the surgeon is prepared as for any other surgical procedure, a preparation which should include masking. An assistant removes the protective dressing and prepares the skin margins of the wound by cleaning with ether to dissolve the fat, so that the adhesive will stick. Care must be exercised when applying skin antiseptic not to allow it to come in contact with the delicate intestinal serosa. If evisceration has occurred in an infected field, or has been unrecognized for several hours, it may be well to lavage the protruded viscera with warm normal saline solution. Gauze dress-

ings moistened in saline may now be applied over the intestine. It is well to use at least three thicknesses of gauze dressing so that the superficial layers can absorb the serous discharge which always occurs. The gauze dressing lying next to the intestine should not be removed or replaced until it has loosened itself from serosa, a process that will require four or five days. Flamed one-inch adhesive strips are prepared by a nurse and applied by an assistant, who removes his gloves. The strips should be long enough to grasp the full width of the abdominal wall. They should be applied first over the center of the protrusion; one then works both up and down to the extremities of the wound. Firm pressure should be applied, and effort should be made to reduce the evisceration and coapt the wound margins. This will rarely be possible, but with succeeding daily dressings, the edges of the wound can be brought together gradually. In certain instances, injection of 0.5 per cent novocain into the wound margins will aid these manipulations. It is important to change the adhesive daily because there is always some loosening due to the slipping of the strips or further reduction of the protrusion. When applying fresh adhesive strips, the same aseptic precautions as for the first dressing must be exercised, and reopening of the wound must be prevented by removing and replacing the strips one at a time. Absorbent gauze pads are placed over the adhesive strapping, and further support is supplied by a firm abdominal border.

If it is possible to bring the wound edge together at once, healing will occur just as rapidly and just as soundly as when sutures have been employed. But when coaptation is effected gradually, healing will be slower and incisional hernia is more certain to ensue than if closure had been obtained by sutures.

AFTERTREATMENT

Aftertreatment, regardless of the method of closure, should begin with a blood transfusion. Ileus is of such frequent occurrence that the indwelling duodenal catheter should be used on all patients with wound disruption, since the earlier treatment is begun, the more likely it is to be effective. In our experience, intestinal obstruction has been due more often to inflammatory than to mechanical ileus. The former yields to hot stupes and continuous duodenal suction drainage, but the latter is a definite indication for operative intervention.

Mechanical obstruction is, of course, the one definite contraindication to nonoperative treatment. However, since the exact nature of the obstruction is not always apparent, there is nothing lost by conservative treatment, since, even if operation is definitely indicated later, the supportive measures already instituted will enable the patient to better withstand surgical intervention. Vitamin C,[5] because of its value in

promoting wound healing, should be given in dosages of 300 mg. per day because smaller doses are ineffectual. Hypoproteinemia is combatted by repeated small blood transfusions, but if the blood concentration is at or near normal and the serum protein and serum globulin are below normal, blood plasma should be administered. The recent work done with lyophile serum[8] and intravenous amino acids[2] perhaps opens up a new field of therapy, but we have had no experience with administration of these substances.

COMMENT

In 1936 I reviewed all the recorded cases of wound disruption at the Henry Ford Hospital up to and including the year 1935.[3] The mortality rate of 34 per cent, while appalling, was not out of line with other published reports. A detailed study of the fatal cases yielded the thought-provoking observation that 70 per cent of the patients who died did so within twenty-four hours of being subjected to operation for secondary closure. The inference then must be that, in certain cases at least, the operation itself was a determining factor in the fatal issue. This does not mean that all the patients would have recovered if the disrupted wound had not been operated upon, for many of them were doomed because of the condition that required surgical interference in the first place and from other complications. However, it does suggest that alternative methods of management of wound disruption should receive serious consideration.

Since the beginning of 1936 we have treated at the Henry Ford Hospital twenty-seven cases of wound disruption occurring in 4,153 laparotomies, an incidence of only 0.65 per cent. The mortality rate for this small series was 37.3 per cent and compares favorably with 34 per cent for our former series; but what is more significant is the evidence in favor of nonoperative treatment. Seven of the sixteen patients whose wounds were resutured died, a mortality of 43 per cent, but only three of the eleven patients whose wounds were treated by adhesive strapping died, a mortality of only 27.3 per cent.

It will always be difficult to introduce statistical evidence in favor of nonoperative measures because the tendency is to restrict their use to the more seriously ill group of patients where the mortality is certain to be high with any form of treatment. However, the evidence in favor of the nonoperative treatment of wound disruption in our own cases has resulted in a reversal of our former practice of operating upon all patients as soon as the diagnosis was established. Secondary suture has gradually been abandoned until, in the past two years, all instances of wound disruption occurring on the general surgical service have been treated by packing and adhesive strapping—a course that in our hands has yielded excellent results.

CONCLUSION

A plea is entered for the wider adoption of conservative treatment in abdominal wound disruption. The high mortality following secondary closure is caused in part by a desire to treat the existing emergency rather than the patient.

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POSTOPERATIVE SHOCK DUE TO HEMOLYTIC STREPTOCOCCUS WOUND INFECTION

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THE essential features of secondary or traumatic shock may be produced by various noxious forces, and usually such harmful influences are present in combination. The state of "vascular failure"[1] accompanying reduction in circulating blood volume, hemoconcentration, and lowered systolic blood pressure, when appearing soon after operation, usually signifies to the clinician disturbances of homeostasis by a conspiracy of harmful agents. It is the purpose of this report, however, to draw attention to the syndrome of postoperative shock depending on a particular cause, fulminating infection of the wound with hemolytic streptococcus. Early recognition of the true nature of the condition is of lifesaving importance, and specific treatment of the infection rather than symptomatic treatment of shock is urgently indicated.

CASE 1.—S. P., a 37-year-old woman, was admitted to the hospital for surgical collapse therapy for chronic pulmonary tuberculosis with cavitation. Nine months previously the patient had undergone upper thoracoplasty on the right in two stages with good results. She had shown much improvement, with gain in weight and strength and diminution in cough and sputum. She was readmitted for treatment of cavitation at the left apex. Her general physical condition was excellent, and there was no extrathoracic abnormality of significance. The heart appeared normal; the blood pressure was 120/80. There was a mild coryza, in view of which the operation was postponed for three weeks. The red cell count was 4.5 million, the hemoglobin 80 per cent. The urine contained albumin, but was otherwise negative.

On Jan. 28 left upper thoracoplasty with removal of three ribs was performed under nitrous oxide-oxygen-ether anesthesia without difficulty, there being no untoward reaction. Next day, twenty-four hours after operation, the patient went into a state of collapse, with systolic blood pressure of 60, cold clammy extremities, slight cyanosis, and rapid small pulse. Diagnoses considered by the house staff were hemorrhage into the wound, pericardial effusion, pneumothorax, or pleural effusion. The patient was mentally alert and appeared to have no particular discomfort. A chest film was made, but gave no help in diagnosis. Blood transfusion and saline solution infusions were given.

On Jan. 30 the patient's condition was unimproved, the state of shock having continued unrelieved. The rectal temperature was 104°; the white cell count was 36,000, and the operative wound now came under suspicion. Externally the wound looked innocent, but the fluid aspirated was found on smear to contain numerous gram-positive cocci, and culture yielded a heavy growth of hemolytic streptococci. Further transfusions were given, but the peripheral vascular collapse continued, and the patient died Jan. 31, three days after operation. There was no autopsy.

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CASE 2.—S. C., a 39-year-old woman, was admitted to the hospital for surgical collapse therapy, the diagnosis being bilateral pulmonary tuberculosis and left tuberculous empyema. The patient had developed tuberculous empyema during pneumothorax treatments; the fluid contained no organism except the tubercle bacillus. At physical examination the patient's general condition was found to be fairly good, and no extrathoracic abnormality of importance was present. The cardiovascular status was excellent. The red cell count was 4.8 million; hemoglobin, 85 per cent. The white cell count was 9,600, and the smear showed 56

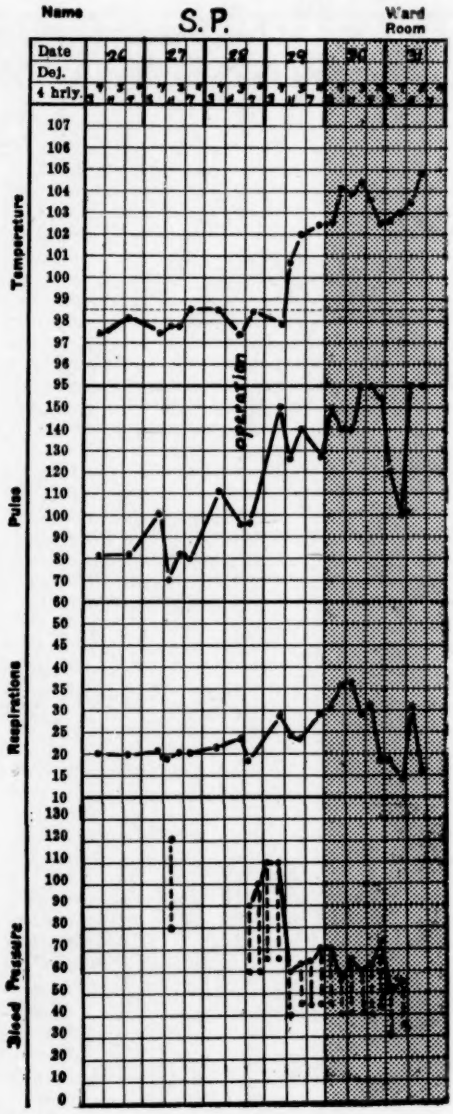

Fig. 1.

per cent polymorphonuclears, 35 per cent lymphocytes, 8 per cent monocytes, and 1 per cent eosinophiles. The urine was negative. Chest x-ray study showed the right lung clear and the left atelectatic beneath pyopneumothorax.

On March 24 left upper five-rib thoracoplasty was performed without incident under nitrous oxide-oxygen-ether anesthesia. The patient stood the operation well and was in good condition at its conclusion. Next day, thirty hours after

operation, a sudden alarming drop in the patient's blood pressure was noted. The blood pressure was 70/40; the extremities were cold and clammy; the pulse was rapid and feeble. Diagnoses considered were hemorrhage into the wound and tension pneumothorax. Aspiration of the wound and left pleural cavity excluded these possibilities, but the fluid was not examined bacteriologically, as infection of the wound was not suspected. On March 26 the patient's condition was worse and the vascular collapse persisted despite blood transfusions. The steadily rising temperature

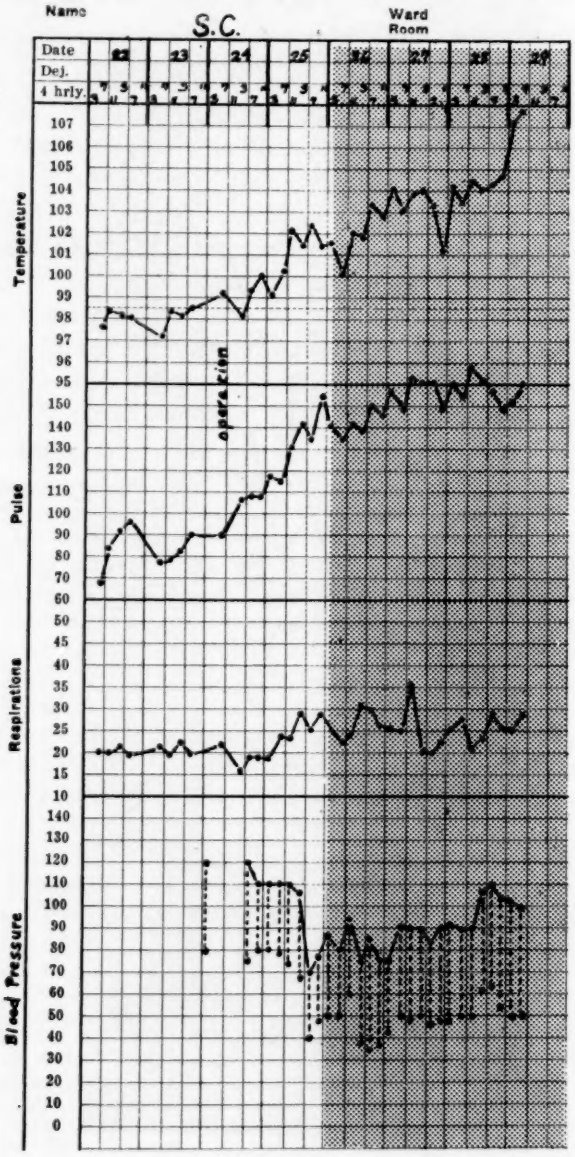

Fig. 2.

and pulse rate and the presence of induration where the skin was penetrated during chest tap the day before suggested wound infection. The wound was opened and serosanguineous fluid containing hemolytic streptococci in abundance was evacuated. The patient's condition steadily failed, however, and death in hyperpyrexia occurred five days after operation. Autopsy showed bilateral pulmonary

tuberculosis, left encapsulated tuberculous empyema, hemolytic streptococcus infection in the thoracoplasty wound, and hemolytic streptococcus bacteremia.

CASE 3.—M. C., a 62-year-old woman, was admitted to the hospital for surgical treatment of carcinoma of the left breast, noted eight weeks previously. Admission had been postponed for two weeks on account of a severe upper respiratory infection. The patient's general condition was excellent on admission. The nasopharynx and

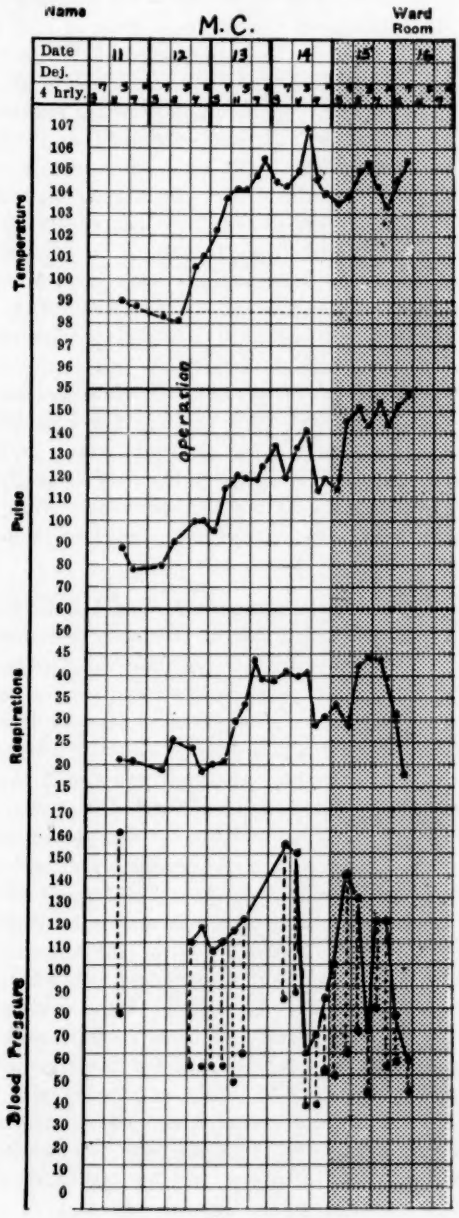

Fig. 3.

bronchi showed no evidence of persistent respiratory infection, and chest x-ray study was negative. The blood pressure was 160/76 and the heart seemed normal. There was a mass retracting the nipple of the left breast, but the skin did not appear to be directly involved and there was no ulceration or dermatitis. No involvement of

the axillary nodes could be made out. The temperature was normal; the white cell count was 10,100, with normal differential values, and the red count was 4.9 million. The urine was normal.

On March 12 left radical mastectomy was performed under ether anesthesia and the wound was closed without drainage. There was considerable blood loss during the operation, and at the end of the operation the patient's blood pressure had declined from 160/80 to 80/50, and there was other evidence of mild shock. The response to infusion of solution of 10 per cent glucose and 0.9 per cent sodium chloride was rapid, however, and the same evening the patient's condition was good, though the blood pressure was slow in returning to the preoperative level. Next day, twenty-four hours after operation, the rectal temperature was 104° and the pulse rate was 120. The wound was examined and appeared satisfactory. Indefinite signs at the base of the right lung were interpreted as indicative of consolidation and explanatory of the fever. On March 14, forty-eight hours after operation, the patient suddenly developed the signs of severe shock, and in three hours the blood pressure dropped from 150/86 to 60/36. The extremities were cold, wet, and grayish. The mental reactions were interesting, the patient being alert, quickly responsive, and somewhat exhilarated. The wound was opened and 2 or 3 ounces of dark reddish fluid containing numerous streptococci was evacuated. The wound was packed open with gauze moistened in physiologic salt solution; blood transfusion was given and administration of prontosil parenterally was begun. Blood cultures were positive for hemolytic streptococci, and cultures of fluid from a bleb on the leg gave abundant growth of the same organism. The patient's condition steadily failed; the hyperpyrexia continued and she became delirious and died four days after operation. Autopsy showed hemolytic streptococcus infection of radical mastectomy wound with bacteremia and early bilateral bronchopneumonia.

CASE 4.—H. M., a 48-year-old woman, was admitted to the hospital for diagnosis and treatment of persistent dull pain in the lower abdomen of two years' duration. Seventeen years previously right transperitoneal nephrectomy had been performed for hypernephroma. Seven years before admission excessive uterine bleeding had been treated by production of artificial menopause by irradiation. Her recent health had been good except for chronic lower abdominal ache, worse in the right lower quadrant. Her general physical condition was found excellent; there was no pulmonary or cardiovascular abnormality, and the blood pressure was 135/70. Laboratory studies, abdominal scout films, and intravenous pyelography were negative.

On Dec. 16 exploratory laparotomy, appendectomy, and excision of the lower two-thirds of the previous laparotomy scar were performed under ether anesthesia. There were adhesions beneath the laparotomy scar and the appendix was fibrotic and thickened, though not acutely inflamed. The stump of the appendix was carbolized but not buried. Next morning the patient's condition seemed alarming. Her rectal temperature was elevated, but her extremities were cold and clammy and the blood pressure was 74/40. She seemed to have no pain and was mentally clear. The attending surgeon was unable to account for the state of shock, but ordered a blood transfusion to be done. The white cell count was 26,500; the red cell count was 4.2 million, and in the smear many young polymorphonuclear forms were seen. The patient's vascular collapse was somewhat benefited by blood transfusion and saline solution infusions, but her condition continued to be precarious. Thirty-six hours after operation an internist in consultation made a tentative diagnosis of acute adrenal insufficiency from hemorrhage into the adrenals. Cortical extract was administered, and a second blood transfusion was given the patient.

On Dec. 18, forty-eight hours after operation, the patient suddenly developed signs of severe shock, the blood pressure falling to 50/38. A second consultant

agreed with the tentative diagnosis of acute adrenal insufficiency and suggested also the possibility of pulmonary embolism and auricular fibrillation. Digitalis was administered, and an electrocardiogram showed auricular tachycardia with varying degree of auriculoventricular heart block. A cardiological consultant, however, favored a diagnosis of pulmonary embolism. Oxygen therapy was instituted. Seventy-two hours after operation blood cultures taken twenty-four hours after operation were reported as showing heavy growth of hemolytic streptococci.

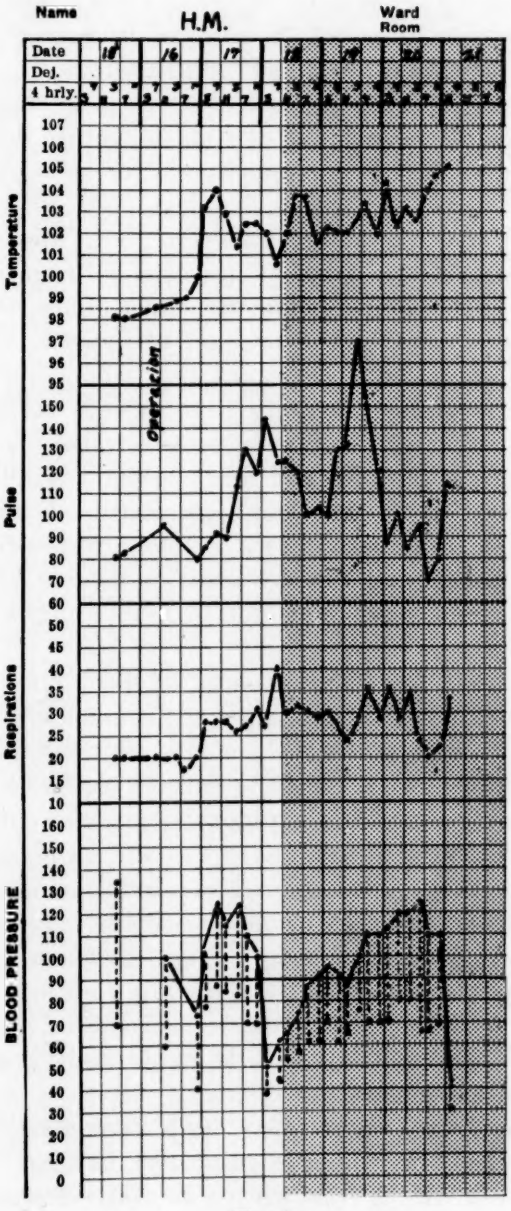

Fig. 4.

Another consultant interpreted the picture as classical of peripheral endophlebitis with septic infarction of the lungs and began sulfanilamide and antibacterial antibody therapy, but on the following day the patient died, five days after operation.

The autopsy showed hemolytic streptococcus peritonitis and bacteremia, acute periphlebitis and lymphangitis of the left leg, and acute serofibrinous pleuritis. The adrenal glands were normal.

Discussion.—The charts of rectal temperature, rate of pulse and respiration, and systolic and diastolic blood pressure, determined at three-hour intervals, are shown for each case (Figs. 1-4). Heavy black ink is used in the charts up to the point of onset of shock, while cross-hatching is used thereafter, to bring out the contrast between the appearance of the chart at the time shock set in and terminally.

These cases have in common the sudden onset of shock within forty-eight hours after extensive operations on previously uninfected tissues. In each instance the infecting organism was the hemolytic streptococcus and the outcome was fatal within five days. The patients were under close observation and the manifestations of shock appeared with startling abruptness. Such evidence of infection as fever and leucocytosis was not distinct enough at the time vascular collapse developed to suggest the true diagnosis to the medical attendants, and it was only twenty-four hours or more afterward that wound infection was suspected. In the meantime the state of shock was variously attributed to hemorrhage, pulmonary embolism, acute adrenal insufficiency, pneumonia, auricular tachycardia and heart block, multiple septic pulmonary infarcts, tension pneumothorax, pericardial tamponade, or to a combination of such factors. All such etiological possibilities were excluded by the clinical and autopsy findings, leaving no doubt in these cases that shock and death were due to fulminating streptococcus infection.

It is a well-known fact that the onset of shock may mark the progress of overwhelming infections, such as pneumonia,[2] diphtheria,[3] and gas gangrene,[4] though, as Warfield points out,[5] the failure of circulation is often erroneously ascribed to cardiac weakness. The essential feature is probably reduction in venous return and cardiac output dependent on widening of the capillary bed and on plasma loss into the inflamed areas.[6] The importance of the factor of increase in size of the capillary bed is evidenced in the cases being reported above by the rapidity with which the circulatory collapse developed. Whether such capillary paralysis results from the sudden release into the general circulation of large amounts of bacteria or bacterial toxins, which act directly against the capillary wall, is an interesting question of considerable prognostic import.

Regarding the source of the infection in these cases, there is no conclusive evidence. It may be of significance, however, that the infections all occurred during the winter months. From this, probable origin in the nasopharynges of those in the operating room may be inferred, but in the absence of studies which might have established the presence of the same strain of hemolytic streptococcus in the nasopharynx of a member of the operating team and in the patient's wound

such an explanation must remain conjectural. All the members of the operating teams were free from upper respiratory infections, and wore standard folded gauze masks which covered mouth and nose. The inadequacy of the usual surgical oronasal mask is notorious, however.[7-9] A practicable method insuring the complete protection of a large wound from air-borne oronasal organisms during a long operation can hardly be said to exist, but progress toward this goal has recently been made.[10, 11] Two of the above cases occurred the same winter. Other factors, such as personnel of the operating teams, preparation of the field of operation, and location of the operating rooms were variable.

These cases were dealt with before chemotherapy and immunotransfusion had become the effective weapons they now are in treating virulent infection due to the hemolytic streptococcus. In Cases 3 and 4 tardy use of prontosil and sulfanilamide in insufficient dosage was made. It can hardly be doubted that recognition of the wound infection immediately after the telltale signs of shock appear in such cases would make it possible to treat them with some success. A fatal delay may result from treating the signs of shock rather than the underlying cause. Immediate aspiration of the wound with examination of the stained smear should lead to immediate diagnosis and proper treatment.

CONCLUSION

Four cases are presented which illustrate the syndrome of postoperative shock due to fulminating infection of the field of operation with hemolytic streptococci. In these cases there was a delay of more than twenty-four hours after the onset of shock before the presence of wound infection was suspected. The urgent need for immediate recognition of the infection in such cases, in order to permit specific treatment by methods of chemotherapy and immunotransfusion, is stressed.

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ORAL AND PARENTERAL USE OF SYNTHETIC VITAMIN K-ACTIVE SUBSTANCES IN HYPOPROTHROMBINEMIA

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ON THE basis of recent laboratory and clinical investigation, the vitamin K potency of certain synthetic naphthoquinones may be regarded as tentatively established.[1-5] Questions which require further study concern the dosage of the naphthoquinones, their toxicity, the need for giving bile salts with them, the choice of oral or parenteral administration, and the duration and uniformity of prothrombin response.

In the present study of thirty patients with hypoprothrombinemia, plasma prothrombin was determined by the method of Warner, Brinkhous, and Smith[6] as slightly modified.[7] The normal value by this method ranges from 90 to 110 per cent, while the zone of dangerous tendency to spontaneous bleeding is below 40 per cent. The 2-methyl-1,4-naphthoquinone and the 2-methyl-1,4-dipropionyl-naphthohydroquinone used were kindly supplied by A. Black of E. R. Squibb & Sons. The water-soluble sodium bisulfite derivative of 2-methyl-1,4-naphthoquinone was synthesized by M. B. Moore and F. J. Kirchmeyer of Abbott Laboratories. The latter substance is probably the sodium salt of the 3-sulfonic acid of 2-methyl-1,4-naphthoquinone. The deoxycholic acid used was furnished by Riedel de-Haen, Inc. As determined by biological assay on the chick, 1.8 mg. of the sodium bisulfite derivative orally administered is equivalent to 1 mg. of 2-methyl-1,4-naphthoquinone, or to 2,500 Peirce-Dann units and 62,500 Dam units.[8] The dipropionyl derivative also is about one-half as active as 2-methyl-1,4-naphthoquinone.[9] The assumption is probably justifiable that the vitamin K potency of these substances is as great given parenterally as orally.

On the basis of treatment the patients may be divided into three groups: those who took methyl naphthoquinone and deoxycholic acid orally; those who took the dipropionyl derivative and deoxycholic acid by mouth; and those who were treated by subcutaneous administration of the sodium bisulfite derivative of methyl naphthoquinone. As shown in Table I, 8 patients were studied while taking daily by mouth 1 mg. of methyl naphthoquinone in corn oil and 0.5 Gm. of deoxycholic acid. The therapy lasted from two to seven days. Six of the 8 patients had initial plasma prothrombin values below 50 per cent, and in 4 of these the response to treatment was excellent. Satisfactory improvement in

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TABLE I

PROTHROMBIN RESPONSE IN VARIOUS DISEASES DURING ORAL ADMINISTRATION OF 1 MG. METHYL NAPHTHOQUINONE IN CORN OIL AND 0.5 GM. DEOXYCHOLIC ACID DAILY

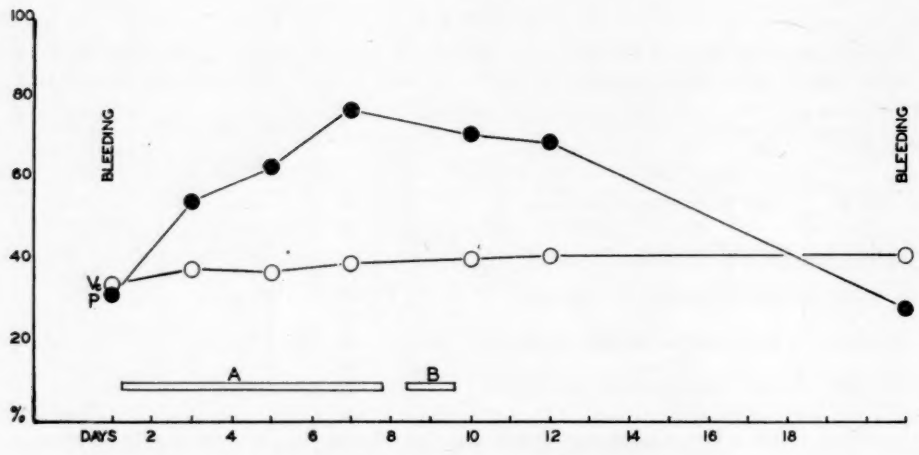
PATIENT	AGE	DIAGNOSIS	DATE	PLASMA BILIRUBIN MG./100 C.C.	PLASMA PROTHROMBIN %
M.M.	54	Common duct stone	11/ 9/39	8.8	48.6
			11/11/39	2.6	76.7
J.C.	37	Common duct stone	3/ 4/40	17.0	44.6
			3/ 8/40		86.2
F.N.	55	Hepatic carcinoma	2/27/40	24.3	52.8
			3/ 4/40	24.0	76.0
B.L.	46	Toxic hepatitis, liver failure	3/ 4/40	27.0	46.3
			3/ 7/40	33.0	42.6
A.H.	54	Portal cirrhosis, liver failure	3/16/40	9.5	43.0
			3/20/40		40.4
G.S.	30	Chronic ulcerative colitis	2/ 3/40	Normal	64.2
			2/ 5/40		68.7
			2/ 7/40		77.9
I.G.	18	Disseminated lupus	2/ 3/40	Normal	32.2
			2/ 5/40		54.7
			2/ 7/40		63.2
M.L.	35	Steatorrhea, regional ileitis	10/ 3/39	Normal	40.0
			10/10/39		95.3

prothrombin concentration also occurred in the 2 patients having initial values between 50 and 75 per cent.

Twelve patients were given orally the dipropionyl derivative of methyl naphthoquinone in corn oil with deoxycholic acid, as shown in Table II. The 1 patient in the group whose initial plasma prothrombin value was below 50 per cent showed rapid improvement. Nine patients had initial concentrations between 50 and 75 per cent and 7 showed improvement under treatment.

As shown in Table III, of the 14 patients receiving parenterally the sodium bisulfite derivative of methyl naphthoquinone, 5 had initial plasma prothrombin concentrations of less than 50 per cent. Of these 5 patients 4 showed improvement within forty-eight hours after a single injection of the vitamin K material. Nine patients had initial values between 50 and 75 per cent, and 7 showed satisfactory response to the treatment.

In considering these results more broadly, of the 20 patients treated by the oral administration of methyl naphthoquinone or its dipropionyl derivative plus deoxycholic acid, 5 failed to show improvement in prothrombin concentration in three to six days of treatment. Four of these 5 patients had severe intrinsic liver disease and died of liver failure. Of the 14 patients given vitamin K substance subcutaneously, as shown in Table III, 2 made no prothrombin response and 1 of these patients died of liver failure. In 1 patient dying of cirrhosis of the liver and liver failure, the plasma prothrombin concentration remained below 50 per cent despite the oral administration of deoxycholic acid in conjunction with methyl naphthoquinone and large doses of crude vitamin K extracted from alfalfa meal, and despite the subcutaneous injection of the sodium



I.G.- DISSEMINATED LUPUS. DURATION OF PROTHROMBIN RESPONSE
A = METH. NAPH.QUINONE 1 MG + DEOXYCHOLIC AC. 0.8 GM ORALLY DAILY
B = SULFONIC DERIVATIVE 3.7 MG S.C. DAILY
Vc = RED CELL HEMATOCRIT IN PERCENT P = PLASMA PROTHROMBIN IN PERCENT

Chart 1.

bisulfite derivative and the intravenous administration of methyl naphthoquinone.

Improvement in prothrombin concentration cannot be expected to persist after cessation of vitamin K therapy, unless the underlying

TABLE II

PROTHROMBIN RESPONSE IN VARIOUS DISEASES DURING DAILY ORAL ADMINISTRATION OF 2 MG. METHYL DIPROPIONYL NAPHTHOHYDROQUINONE PLUS 0.5 GM. DEOXYCHOLIC ACID

PATIENT	AGE	DIAGNOSIS	DATE	PLASMA BILIRUBIN MG./100 C.C.	PLASMA PROTHROMBIN %
N.M.	27	Chronic ulcerative colitis	10/21/39	Normal	65.1
			10/28/39		95.0
B.O.	69	Common duct stone	10/26/39	3.9	87.1
			10/28/39	2.2	96.0
C.H.	54	Biliary cirrhosis	10/11/39	9.4	56.4
			10/20/39		85.8
E.E.	39	Common duct stone	11/22/39	6.0	69.7
			11/25/39	6.0	96.1
K.T.	55	Toxic hepatitis, liver failure	10/18/39	20.0	53.1
			10/20/39	22.0	57.2
W.B.	53	Toxic hepatitis	1/18/40	24.5	51.0
			1/24/40	26.8	96.1
J.H.	77	Carcinoma of common duct	1/24/40	24.6	38.1
			1/29/40	19.0	92.7
A.M.	79	Common duct stone	11/27/39	7.4	72.4
			12/ 1/39	4.9	91.9
C.B.	58	Toxic hepatitis, liver failure	11/16/39	25.6	62.7
			11/20/39	31.6	69.5
			11/22/39	29.2	60.2
W.W.	60	Carcinoma of common duct	12/ 4/39	22.7	59.1
			12/11/39	3.7	81.1
W.B.	36	Hepatic carcinoma	10/26/39	22.2	55.1
			10/28/39	28.2	90.0
R.W.	58	Common duct stone	10/26/39	1.3	78.5
			10/30/39	1.0	78.9

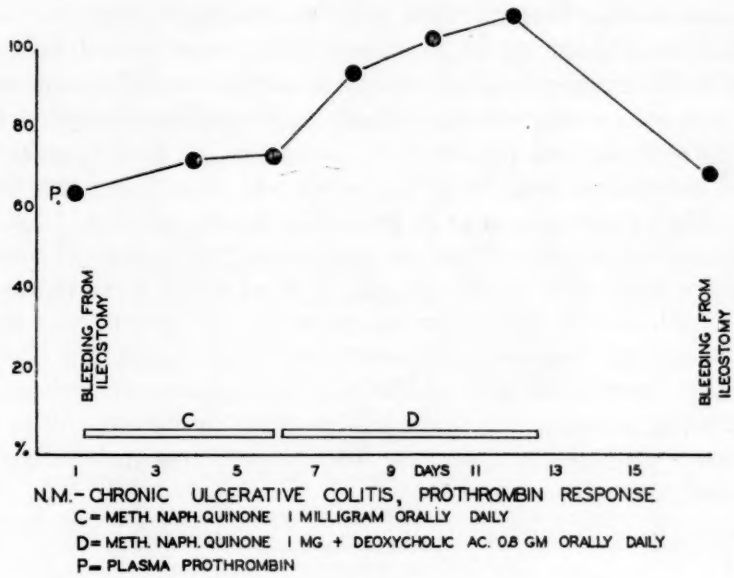


Chart 2.

TABLE III

PROTHROMBIN RESPONSE IN VARIOUS DISEASES AFTER SUBCUTANEOUS ADMINISTRATION OF SODIUM BISULFITE DERIVATIVE OF METHYL NAPHTHOQUINONE

PATIENT	AGE	DIAGNOSIS	DATE	PLASMA BILIRUBIN MG./100 C.C.	PLASMA PROTHROMBIN %	DOSAGE
E. E.	39	Common duct stone	12/ 1/39	1.9	63.4	1.8 mg. s.c.
			12/ 2/39	1.9	95.9	12/1/39
J. Z.	50	Common duct stone	1/27/40	7.2	71.4	1.8 mg. s.c.
			1/31/40		75.0	1/30/40
J. B.	57	Carcinoma of pancreas	12/ 9/39	26.5	11.5	1.8 mg. s.c.
			12/11/39	24.5	92.6	12/9/39
C. B.	58	Toxic hepatitis, liver failure	12/ 1/39	16.9	54.1	1.8 mg. s.c.
			12/ 2/39	21.0	92.2	12/1/39
W. W.	60	Carcinoma of common duct	12/27/39	20.2	51.1	1.8 mg. s.c.
			12/28/39		107.2	12/27/39
M. L.	51	Common duct stone	12/16/39	22.5	68.5	1.8 mg. s.c.
			12/21/39	22.2	90.8	12/20/39
W. B.	53	Toxic hepatitis	2/ 2/40	23.0	73.0	3.7 mg. s.c.
			2/ 3/40	22.0	101.3	2/2/40
R. G.	52	Portal cirrhosis, ascites	3/16/40	14.0	37.0	3.7 mg. s.c.
			3/18/40		38.4	3/17/40
E. D.	60	Common duct stone	3/16/40	Normal	59.2	3.7 mg. s.c.
			3/18/40		76.5	3/17/40
H. C.	34	Portal cirrhosis, hematemesis	4/ 2/40	Normal	48.3	3.7 mg. s.c.
			4/ 4/40		58.9	4/2/40
C. D.	41	Portal cirrhosis, liver failure	4/ 2/40	22.2	42.0	3.7 mg. s.c.
			4/ 4/40		61.5	4/2/40
V. D.	23	Perinephric abscess	2/ 6/40	Normal	53.1	3.7 mg. s.c.
			2/ 7/40		62.7	2/6/40
R. M.	24	Periarteritis nodosa	2/12/40	Normal	34.9	3.7 mg. s.c.
			2/14/40		92.3	2/13/40
H. G.	17	Ileal fistula, intestinal obstruction	4/ 5/40	Normal	57.2	3.7 mg. s.c.
			4/ 6/40		69.5	4/5/40

disease has been corrected. This point is brought out by the data in Chart 1, from the study of a patient with disseminated lupus and pathologic bleeding. This patient took methyl naphthoquinone and deoxycholic acid orally during Period A, while during Period B the sodium bisulfite derivative was given parenterally. Bleeding from the nose and mouth and into the skin was relieved, only to recur when the prothrombin value declined to 30 per cent after cessation of treatment.

The beneficial effects of giving deoxycholic with methyl naphthoquinone are suggested in Chart 2, the data of which were obtained in studying prothrombin changes in an extremely sick patient with chronic ulcerative colitis. This patient was not jaundiced, hence it is of special interest that deoxycholic acid had to be taken with the methyl naphthoquinone orally to restore the prothrombin value to normal. With relief of hypoprothrombinemia, there was definite reduction in bleeding from the ileostomy.

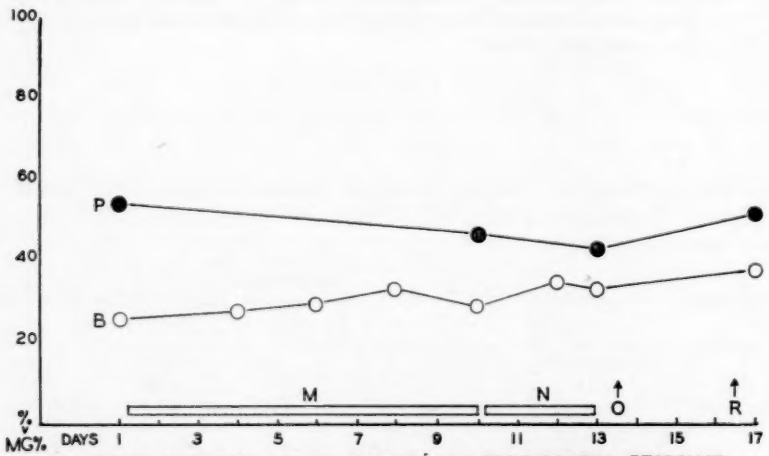


Chart 3.

Prothrombin deficiency may be resistant to treatment in severe hepatic insufficiency, as shown in Chart 3, from the study of a patient with progressive liver failure. The plasma prothrombin values in per cent and plasma bilirubin in milligrams per 100 c.c. are indicated. Neither the oral nor parenteral administration of potent vitamin K-active substances led to improvement in the plasma prothrombin value. Nevertheless, the prothrombin concentration failed to reach extremely low levels, and at no time was there evidence of pathologic bleeding.

Data shown in Chart 4 from the study of a patient with chronic sepsis, prothrombin deficiency, and bleeding from a surgical drainage wound illustrate sluggishness of prothrombin response to intensive vitamin K therapy. The improvement in plasma prothrombin concen-

tration was moderately satisfactory after large doses of sodium bisulfite derivative of methyl naphthoquinone were given subcutaneously. Only small benefit was obtained from the oral administration of methyl naphthoquinone, plus deoxycholic acid, and from the intravenous injection of methyl naphthoquinone. Up to 20 mg. of methyl naphthoquinone, dissolved in 300 c.c. of 0.9 per cent NaCl solution, was given to this patient by vein without untoward effects. The data from this case suggest the futility of giving large doses of methyl naphthoquinone if the usual dose of 1 to 4 mg. per day is ineffective.

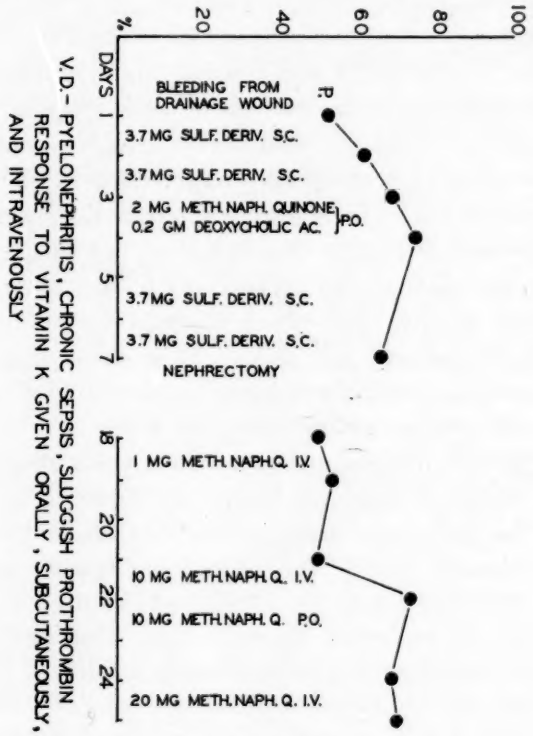


Chart 4.

COMMENT

Sweeping conclusions are not to be drawn in this study, but certain impressions stand out with distinctness. It is clear that prothrombin-lack and an abnormal bleeding tendency may occur in various conditions in which there is no reason to suspect the presence of severe liver disease. Disseminated lupus, steatorrhea, chronic ulcerative colitis, chronic sepsis, and periarteritis nodosa were among the conditions illustrative of this point in the present study. The occurrence of prothrombin deficiency in such varied conditions points up the fact that the fundamental nature of the disturbance is still unknown.

An interesting and puzzling occasional clinical finding is prothrombin deficiency refractory to vitamin K therapy. Failure to respond to

treatment may sometimes be attributable to liver damage of such severity that hepatic synthesis of prothrombin is no longer maintained, even in the presence of the precursor substances. In other cases, however, particularly in chronic sepsis, there may be no evidence on which to incriminate the liver. If one supposes that prothrombin consists of a globulin molecule linked with a vitamin K prosthetic group, then prothrombin deficiency might conceivably depend on inadequate formation of the protein molecule.

Deoxycholic acid and bile salts seem to increase the effectiveness of methyl naphthoquinone when taken orally, even in the absence of jaundice and known intrahepatic disease. Whether this denotes deficient excretion of bile salts and normal pigment excretion in such cases, or whether the synthetic processes in the liver are favorably influenced by ingestion of cholic acid derivatives is a matter for speculation. The point is of considerable importance in choosing between oral and parenteral methods of giving vitamin K. There seems to be no conclusive evidence to cover the question, but theoretically the administration of bile salts in the presence of biliary obstruction may be harmful to renal, hepatic, and other tissues. It is probably wise to give only small amounts of bile salts for the absorption of fat-soluble K-active substances in obstructive jaundice, or else to give preparations suitable for parenteral use and not give bile salts.

The brevity of the prothrombin response after a single dose of vitamin K is worthy of comment. Evidently there is little storage of vitamin K in the body, and sustained effects are not to be expected from a single massive dose if the underlying disease persists. Daily small doses of from 1 to 4 mg. of methyl naphthoquinone, or the equivalent, would seem to be better therapy than occasional larger doses. Such a conclusion is supported by previously published observations on the lability of plasma prothrombin and the need for determining the value frequently in handling cases of obstructive jaundice.[10]

SUMMARY

In a study of 30 patients with miscellaneous diseases and prothrombin deficiency, the following impressions were obtained:

1. 2-methyl-1,4-naphthoquinone, its dipropionyl derivative, and its sodium bisulfite derivative have satisfactory vitamin K-potency taken orally or parenterally in dosage of 1 to 4 mg. daily.

2. No evidence of toxicity was seen in giving as much as 20 mg. of 2-methyl-1,4-naphthoquinone intravenously in one dose.

3. The prothrombin response to treatment appears within twenty-four hours and lasts less than a week after vitamin K therapy is ended. The daily administration of vitamin K is desirable in treating hypoprothrombinemia.

4. Prothrombin deficiency refractory to treatment may be seen in severe liver damage and in chronic sepsis.

5. The effectiveness of 2-methyl-1,4-naphthoquinone taken by mouth is increased by taking deoxycholic acid or bile salts, even in the absence of jaundice.

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RELATIVE MERITS OF THE SCALPEL AND HIGH FREQUENCY CURRENT IN NEPHROTOMY

Experimental Study

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THE increasing trend toward conservative renal surgery, with particular reference to renal lithiasis, and the relatively high mortality rate following extensive nephrotomies prompted this study. That conservative kidney surgery for patients with renal calculus disease is justifiable cannot be doubted. However, as pointed out by Scholl[1] and others, extensive nephrotomy is a hazardous operation due largely to four factors: (1) primary hemorrhage, (2) cortical sepsis, (3) loss of functioning renal tissue by incision or sutures, and (4) secondary hemorrhage.

It was our purpose in this experimental work to study histologically the relative amount of primary hemorrhage, intrarenal extravasation of blood along the lines of incision, infarction of renal tissue, and the relative rate of healing.

Experimental nephrotomies were performed on rabbits with the high frequency cutting current and with the scalpel, two rabbits being used for each procedure. These rabbits were sacrificed at time intervals of two, four, seven, fourteen, thirty, and sixty days. The essential findings of the sections which were taken from the kidney operated upon at various levels will be described below.

De Vincentiis[2] performed a similar experiment and concluded that there was considerably more necrosis extending diffusely into the renal parenchyma from the line of incision in operations in which the high frequency cutting current was used than in operations in which the scalpel was employed. He also noted that healing was retarded somewhat in those cases in which the high frequency cutting current was utilized. Recognizing the advantages of the high frequency cutting current with reference to its hemostatic action, de Vincentiis felt that it should not be employed in kidney surgery for the above reasons. However, as pointed out by Ellis,[3] it should be remembered that a relatively clean cut can be produced with a spark-gap machine by increasing the frequency of oscillation and lessening the amperage.

Before beginning this study, we experimented with the high frequency machine on the kidneys of rabbits until we found the ideal current to be used; that is, one in which the cut was clean with very little evidence of gross coagulation.

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The following is a description of the results we secured in this experimental study:

Fig. 1*A* shows the gross and microscopic sections of the kidney of a rabbit sacrificed two days after nephrotomy had been performed with the scalpel. The line of incision extends from the cortex into the renal

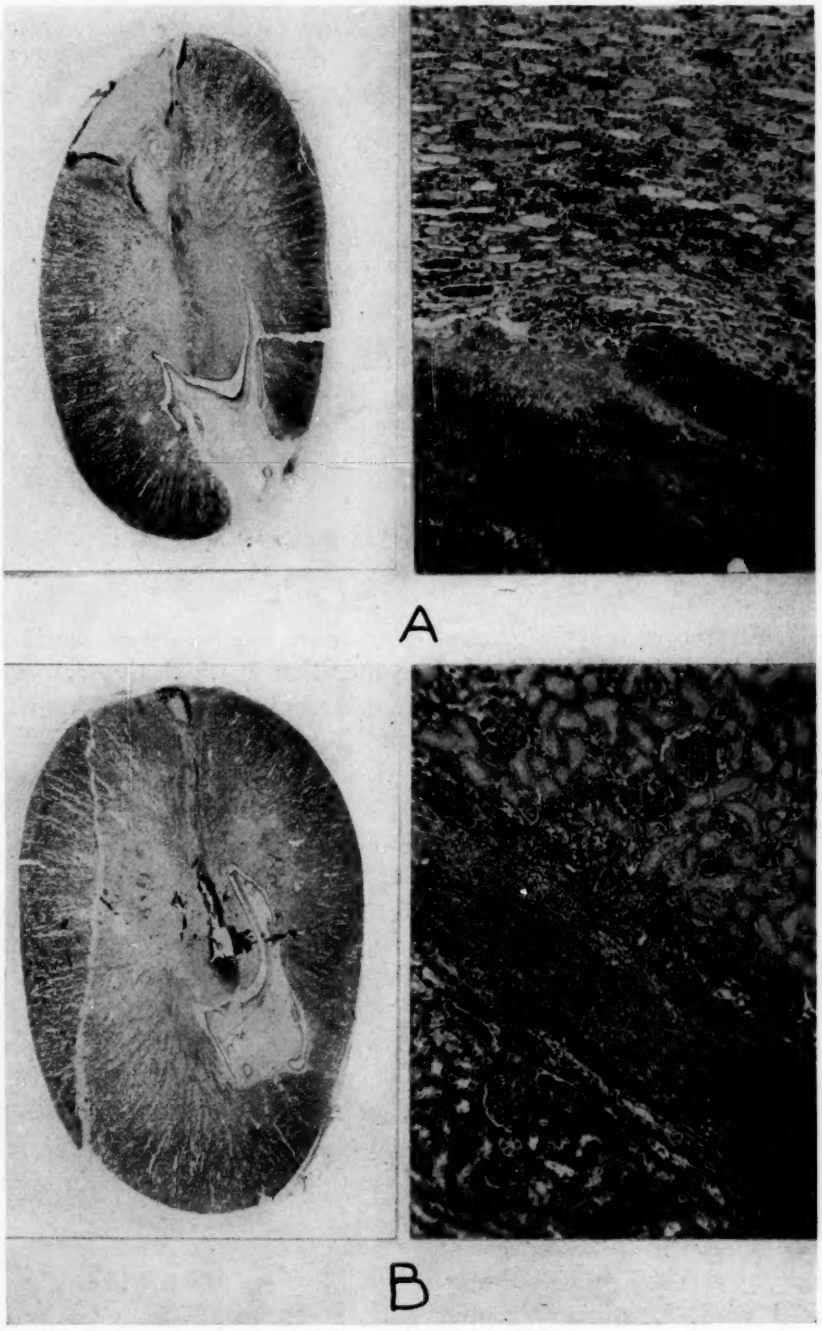

Fig. 1.

papilla and is represented by an extensive area of hemorrhage without evidence of organization. There is extensive extravasation of red blood cells within the kidney tissue adjacent to the line of incision. A large v-shaped area of infarction is present, extending from the cortex into the medullary substance. It is of interest to note that such areas of infarction were more frequently observed in operations in which the scalpel was used in contrast to operations in which the incision was made with the high frequency current.

We believe that there are three definite factors producing such areas of infarction: (1) The site at which the incision is made in the kidney may cut off circulation to a given area; (2) the placing of mattress sutures also impairs renal circulation to definite areas; and (3) with more pronounced degrees of intrarenal hemorrhage seen where the scalpel has been used, there is increasing intrarenal pressure which, we believe, results in impairment of circulation to certain regions. This factor has been consistent in our studies.

Fig. 1*B* represents the gross and microscopic sections from the kidney of a rabbit sacrificed two days after operation which was performed with the high frequency cutting current. The line of incision is represented by a narrow zone of hemorrhage with a small area of infarction in the region of the cortex. Microscopically, the line of incision is sharply demarcated from the adjacent kidney tissue. This condition is to be expected when one considers the coagulating effect of high frequency current where the spark-gap machine is used.

Fig. 2*A* represents the gross and microscopic sections of the kidney of a rabbit sacrificed four days after operation in which the scalpel was used. Fig. 2*B* represents sections from the kidney of a rabbit sacrificed at the same time interval, but in which the operation was performed with the high frequency cutting current. In the sections taken from rabbits operated upon with the scalpel, it is interesting to observe the broader zone of hemorrhage representing the line of incision, associated with a larger area of infarction. An area of necrosis is seen in the tip of the papilla in Fig. 2*A*.

Fig. 3*A* represents the gross and microscopic sections taken from the kidney of a rabbit sacrificed seven days after operation which was performed with the scalpel. A large area of infarction and necrosis is evident in the cortical region. The remainder of the line of incision is barely perceptible except in the papilla where an area of necrosis is discernible. The microscopic section shows quite a broad area representing the line of incision, with no evidence of healing. There is, however, superimposed infection as evidenced by considerable leucocytic infiltration, fibrin, and edema.

Fig. 3*B* represents the gross and microscopic sections taken from the kidney of a rabbit sacrificed seven days after operation which was performed with the high frequency cutting current. The gross section presents an apparently normal kidney with no evidence of red blood cells.

The microscopic section shows the line of incision to be very narrow with evidence of scar tissue formation. The sharp line of demarcation from the incision and the adjacent kidney tissue is again pronounced. Infarcted renal tubules are also seen in this section.

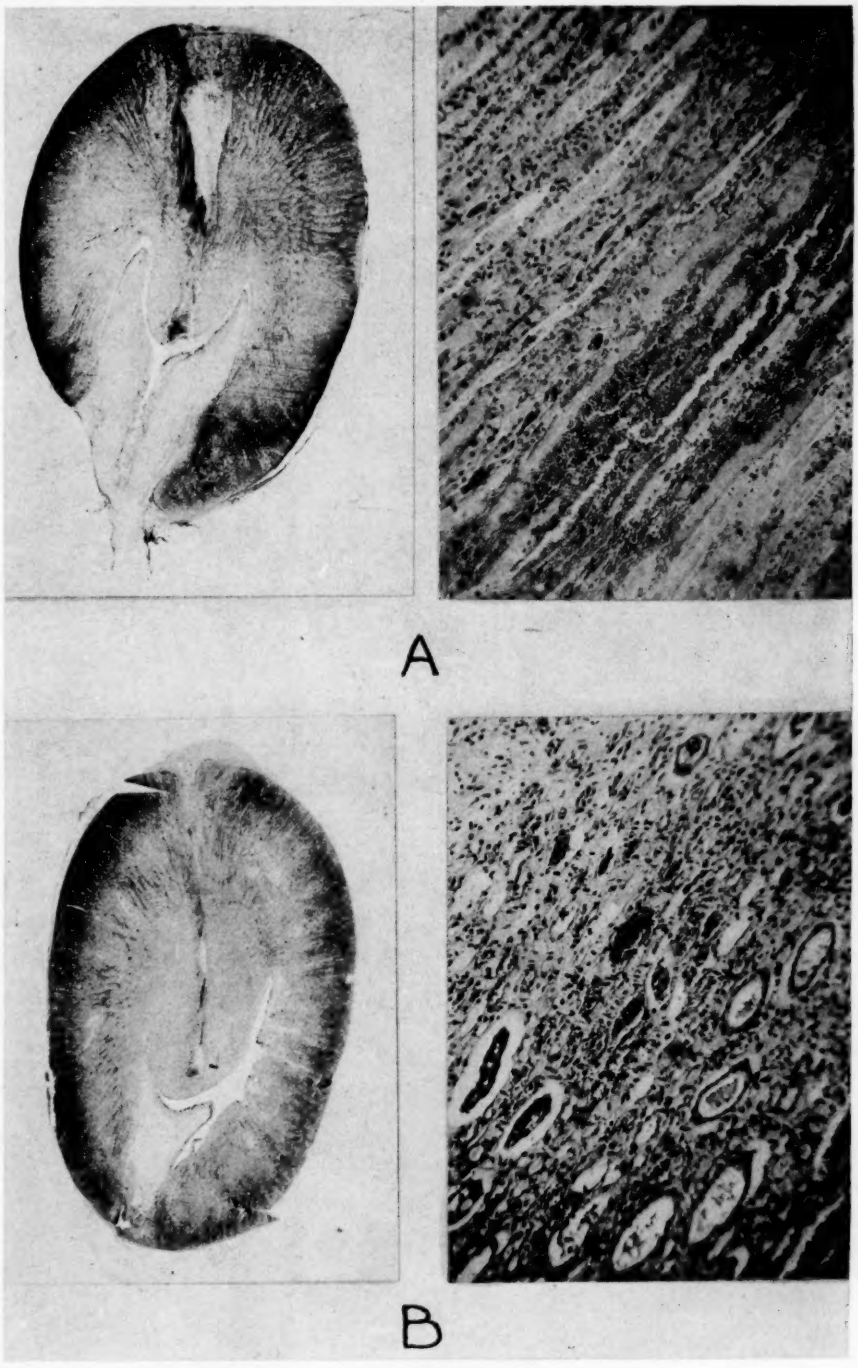

Fig. 2.

Fig. 4*A* represents the gross and microscopic sections taken from the kidney of a rabbit sacrificed fourteen days after operation which was performed with the scalpel. The gross section shows a large area of infarction extending from the cortex into the medullary substance. A suture is seen traversing the area of infarction at its apex and is prob-

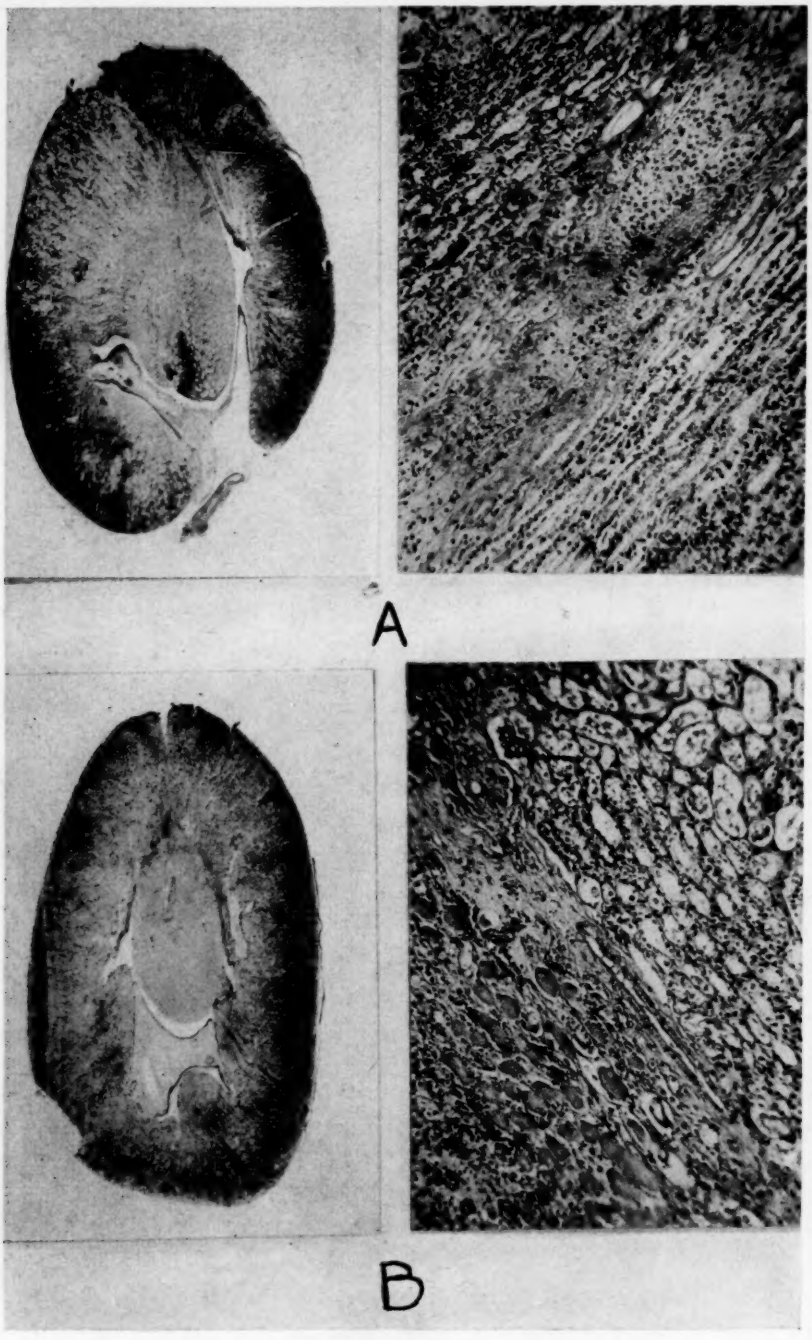

Fig. 3.

ably the etiologic factor producing this infarction. To the right of the infarcted area is a region of atrophy of the kidney tissue which is due to partial impairment of circulation to this region. The microscopic section demonstrates this atrophy of kidney tissue.

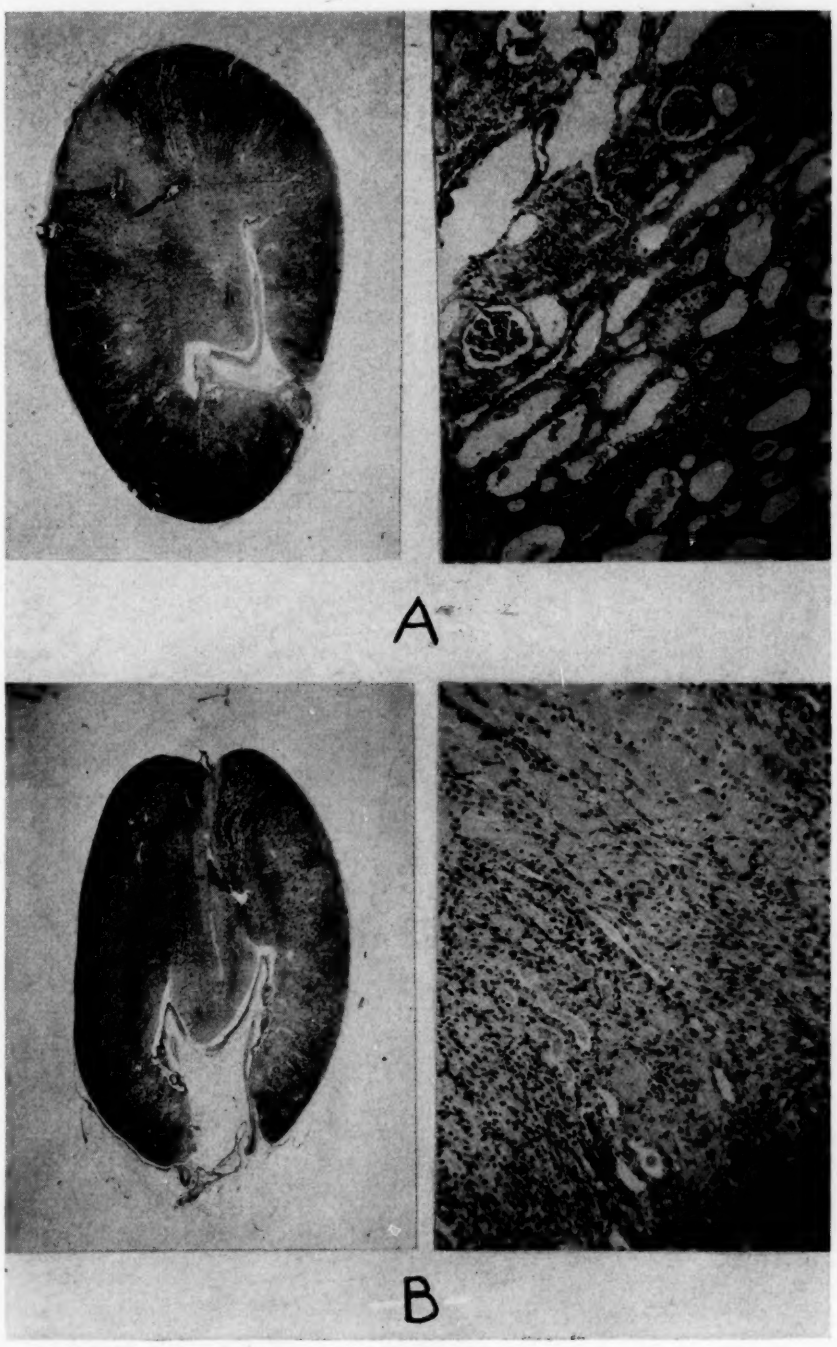

Fig. 4.

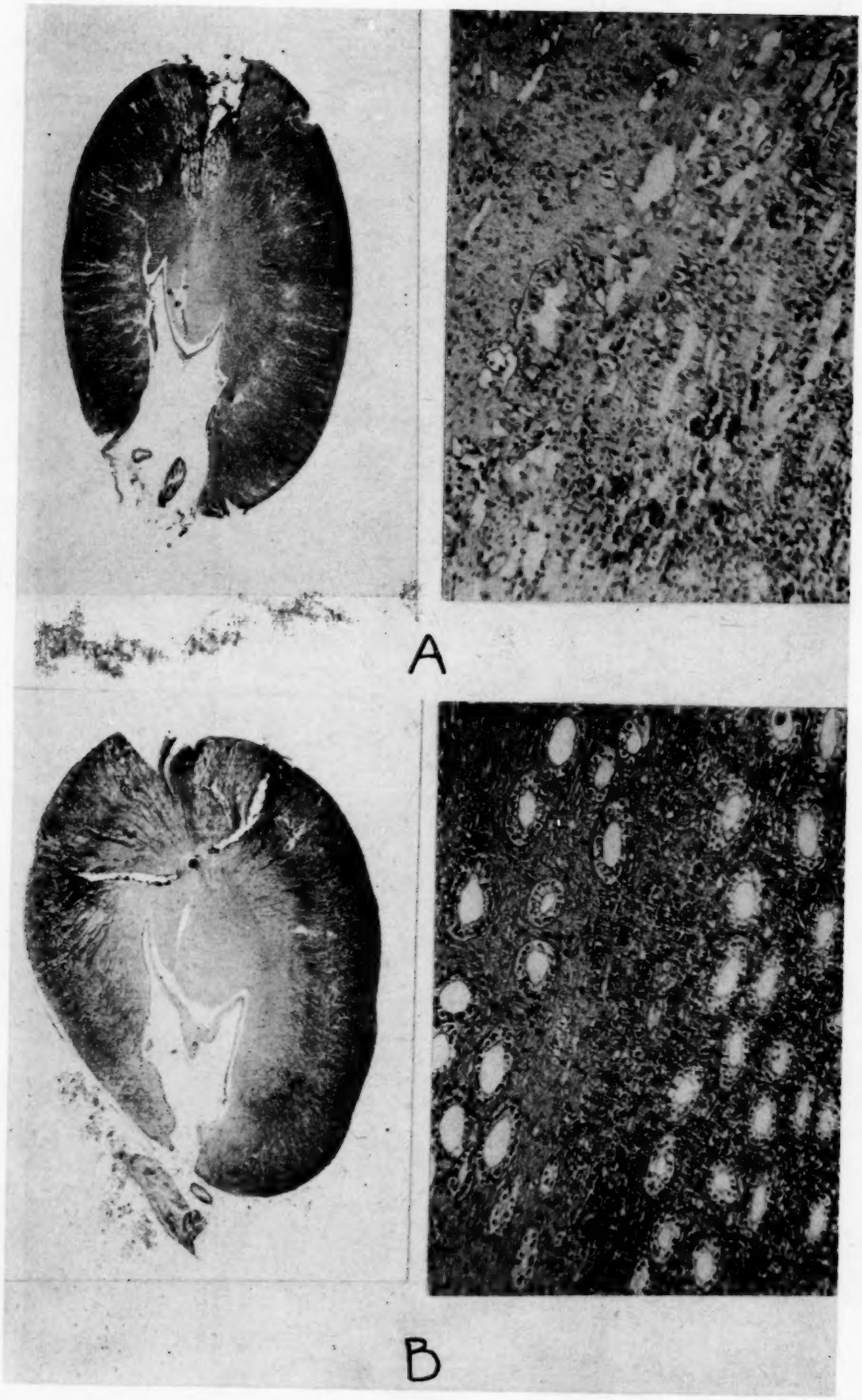

Fig. 5.

Fig. 4*B* shows the gross and microscopic sections from the kidney of a rabbit sacrificed fourteen days after operation performed with the high frequency cutting current. The line of incision is represented by scar tissue formation and a narrow zone of infarction.

Fig. 5*A* represents the gross and microscopic sections taken from the kidney of a rabbit sacrificed thirty days after operation which was performed with the scalpel.

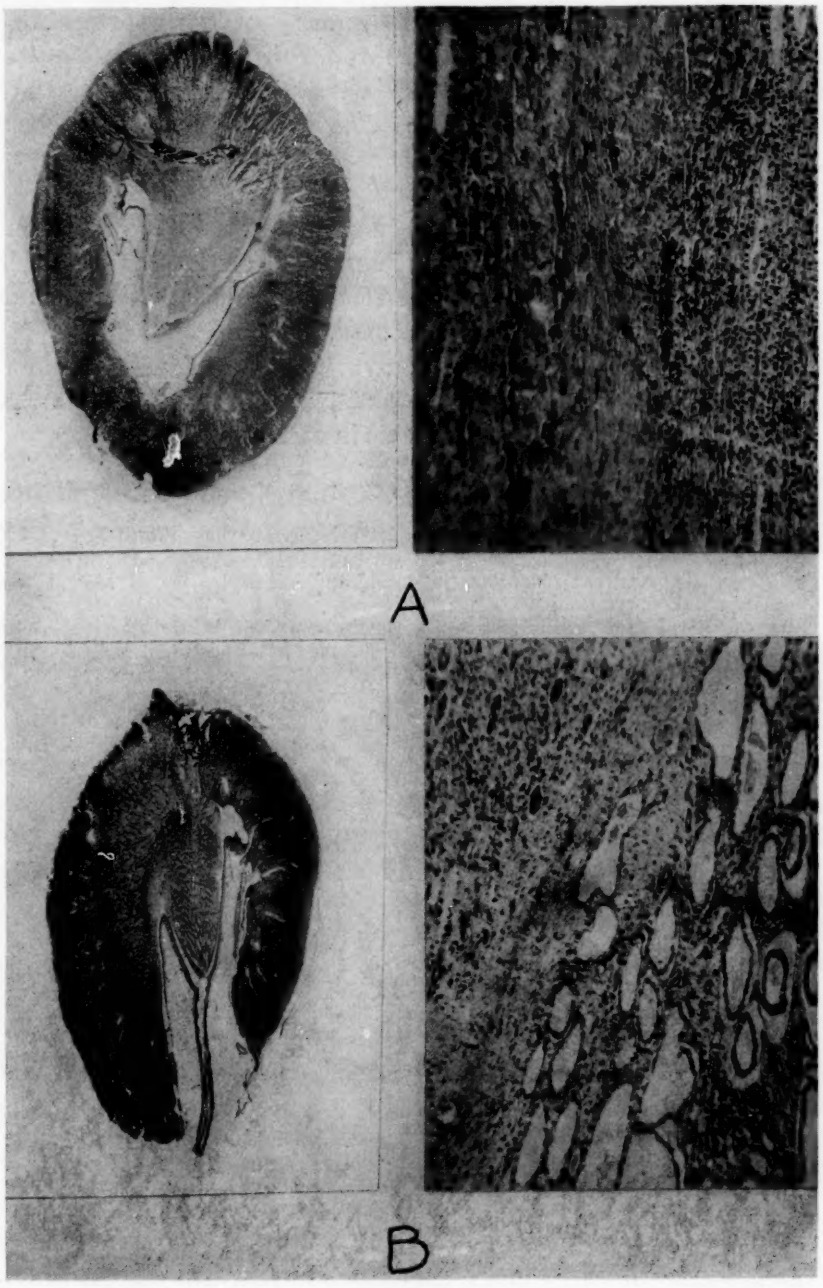

Fig. 6.

Fig. 5*B* represents sections taken at the same time interval, the operation being performed with the high frequency cutting current. The line of incision in both cases is well healed and is represented by scar tissue.

Fig. 6*A* represents sections taken from the kidney of a rabbit sacrificed sixty days after operation which was performed with the scalpel, while Fig. 6*B* shows sections taken from the kidney of a rabbit sacrificed at a similar time interval, the operation being performed with the high frequency cutting current. Again one notes good healing in both cases.

No animals died postoperatively following operations performed with the high frequency cutting current. However, the immediate operative mortality following operations which were performed with the scalpel numbered four animals, all of which died of hemorrhage and shock.

CONCLUSIONS

1. There is less primary hemorrhage when an extensive nephrotomy is performed with the cutting current than when the scalpel is used.
2. Extravasation of blood into the renal tissue adjacent to the line of incision is greater when the scalpel is used.
3. There is less infarction adjacent to the line of incision when the high frequency current is employed.
4. Healing is more or less comparable in each case.

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Editorial

Anesthesia in Medical Preparedness Program

IN THE present preparedness parade the surgeon must march in the front rank. However much we may deplore it, preparations for war mean preparations to furnish the surgeon with unlimited numbers of injured people for whom he must care. In the rush of plans to transpose surgery from a peacetime to a wartime basis, a certain element of hysteria is likely to creep in. We are apt to lose sight of details of prime importance. The matter of anesthesia is one such detail. In civil practice every surgeon has provided himself with what he believes to be a satisfactory solution of the anesthesia problem. Transferred to military duty, he can scarcely hope to take with him an intact surgical team as he has organized it at home. Even if this were possible, anesthesia for mutilated fighters and their victims is a more complicated problem than civilian practice of the relief of pain. The care of respiratory embarrassment in a patient in a civilian hospital is difficult. When the face is shot away or the pleural cavity laid open, maintenance of the respiratory function taxes the skill of the most adept.

We ought to profit by previous experience. In our own army in France in the summer of 1918, after a breakdown in anesthesia service, it was decided that more medical men must be especially trained in anesthesia. Field schools of anesthesia for medical officers were established at camps in this country, but without facilities for practical instruction in operating rooms. Peace came too soon to observe the benefits of such instruction. The arrangement of space used for surgery in France in 1918 was found to be important. Large operating rooms in which several surgical teams could work simultaneously proved of advantage for several reasons, one of which was that one capable anesthetist thus simultaneously can supervise several anesthetized patients when necessary. A similar plan has been found useful in England during the past year. The following quotation from a personal letter from London is pertinent:

"One huge ward at Epsom has been converted to take 6 operating tables . . . At St. Thomas' Hospital we have a very nice emergency theatre, providing for 5 tables in a row with sliding curtains between . . . The usual military practice here is for a full colonel to be in charge of a hospital in a purely administrative capacity. Then there is a lieutenant colonel in charge of medicine and another in charge of surgery who actively run and direct everything apart from administration. Below them the personnel is much the same on the two

services. Take the surgical side: Two majors are general surgical specialists. One major is an anesthetic specialist with additional captains and lieutenants according to the size of the hospital. The anesthetist major is responsible for his underlings, and they may run 6-9 tables.''

The number of physicians in the United States well trained in anesthesia is now much greater than in 1918. Nevertheless, special courses of instruction ought to be established at once so that young medical officers already partly trained and those wishing to render such service may be especially prepared for wartime duty.

In the long past anesthesia has been looked upon as an operating room service solely. The term ''anesthesiology'' has been utilized in recent years to designate a larger service. It includes skill in the use of the various technical maneuvers and drug administration found useful in putting patients ''at ease'' during surgery, but it goes much further than that. The supervision of physiologic processes, especially the function of respiration, during depression following head and chest injuries; after drug administration for pain relief; after gas poisoning; in shock and in pneumonia, involves the use of methods familiar to the anesthetist. The insertion of artificial airways in the presence of blood and mutilation of the respiratory tract, the administration of artificial atmospheres, the cleansing of the tracheobronchial tree when contaminated, artificial respiration, the injection of locally acting anesthetic drugs to relieve the pain of fractured ribs and other bones, all these are technical procedures familiar to the well-trained anesthetist and useful for the safety and comfort of the injured. In military practice such service ought often to be rendered under field conditions. The need for medical officers especially trained along these lines is obvious.

It is highly desirable that those who are formulating plans for medical military preparedness may include the assignment of at least one well-trained physician as anesthetist to each hospital unit. Arrangements ought also to be made for the training of an adequate number of medical officers in anesthesiology so that surgeons may be left free of the worry of providing such service for themselves. It is to be hoped that the present mobilization may include provision for such special training and assignment of medical officers from the beginning, without waiting for the demonstration of such need after field operations have begun.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

RECENT ADVANCES IN THE STUDY AND MANAGEMENT OF TRAUMATIC SHOCK

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I. INTRODUCTION

SHOCK is a subject that is of importance not only during war but in peacetime. It is the major cause of death in all types of injuries and is at present a limiting factor in the operability of many conditions. Surgery has advanced rapidly during the past century when one by one the shackles of pain (anesthesia), infection (antisepsis and asepsis), and, more recently, thrombosis (heparin) were removed. If the danger of shock were out of the way, it is difficult to predict how much the range of operability of morbid processes might be increased.

To review the entire literature on shock would be a herculean task beyond the scope of the present paper. Advances both in the understanding and treatment of shock have been so rapid during the past decade that this review will consider mainly the advances made in that period, 1930 to 1940. This is especially advisable because certain papers appearing at the beginning of the decade brought fresh light to the old subject, the cause of shock. It will be impossible to deal immediately with these most recent advances without a brief historical résumé as a point of departure.

HISTORICAL RÉSUMÉ

A better idea of the advances made in an understanding of shock during the past decade can be had after a brief historical résumé of previous work. Not only is this true because of the contrast in ideas in many cases, but because in others the older workers really laid better foundations for present knowledge than casual study would lead one to realize. It might be interesting arbitrarily to divide the history of shock into four periods.

1. *Early Period.*—From the time of James Latta (1795), of Edinburgh, who used the word "shock," and other early writers down to the time of Fischer (1870) may be considered the *descriptive period.*

2. *1870 to 1898.*—These years involved much speculation and some experiment. Most of the theories propounded during this period implicated nervous impulses as being the cause of shock. Fischer (1870), whose work may be said to have introduced the period, believed in vasomotor exhaustion and stagnation of blood in the splanchnic areas. The latter theory is fallacious and probably originated in the fact that in intestinal manipulation shock stagnation occurs because of local fluid loss (early workers showed as much as 37 per cent stagnation), but in shock of other types does not occur, as shown by the clinical observations of Wallace, Fraser, and Drummond (1919). During this period Gussenbauer's review and other work included the following:

Early experimental observations on the blood dilution accompanying hemorrhage and concentration associated with shock were made by Sherrington and Copeman (1893). Turck (1897) recognized the importance of chilling in the production of shock and devised an apparatus to irrigate with warm (130° F.) water the stomachs of patients operated upon.

3. *The Experimental Physiology Period, 1899 to 1923.*—The work of this period was introduced by Crile's first book, climaxed by the studies of the Shock Committee during World War I and summarized by Cannon's monograph in 1923. The article of Power (1906) gives an idea of the views early in this period.

Following this there was a period of relative inaction, before the final period.

4. *The Experimental Clinical Period, 1930 to 1940.*—These last two periods are discussed in more detail below. Heinemann (1938) has given an excellent résumé of the history of shock.

The Exhaustion Theory of Shock, the Crile-Mummery Hypothesis.—One of the differences between Crile's work and that of others was that, instead of propounding his theory in a series of articles, he advanced it in a series of books. Crile has published almost as many books on shock as all other writers combined. All of these books contain data to support his exhaustion theory, which is also propounded in a series of articles, including those of Crile (1923), Crile (1924), and Crile, Rowland, and Telkes (1928).

The views of Crile may be seen most readily by reading the following quotation from one of his articles (1924): "The body as a whole is an electro-chemical mechanism, the positive pole being the brain, the negative the liver, the connecting wires the nerves, the salts in solution the electrolytic fluid in which the electro-chemical mechanism is immersed. When either pole, i.e., the liver or the brain, is removed or destroyed, the organism perishes."

Crile and Hosmer (1919) reported that in shock the electric conductivity of the brain is decreased and that of the liver increased.

TABLE I

THEORIES OF SHOCK

1. Nervous
   - Vasomotor exhaustion
     - Mitchell, Morehouse, and Keen (1864)
     - Fischer (1870)
   - Exhaustion
     - Crile (1897-1920)
     - O'Shaughnessy and Slome (1935)
   - Inhibition
     - Meltzer (1908)
2. Fat embolism
   - Bissell (1917)
   - W. T. Porter (1917)
3. Arterial vasoconstriction and capillary congestion
   - Mapother (1879)
   - Malcolm (1893-1909)
   - Starling (1918)
   - Erlanger, Gesell, and Gasser (1919)
4. Acapnia
   - Henderson (1908)
5. Acidosis
   - Cannon (1919)
6. Hyperactivity of adrenal medulla
   - Bainbridge and Trevan (1917)
   - Freeman (1933)
7. Exhaustion of adrenal medulla
   - Sweet (1918)
8. Adrenal cortical insufficiency
   - Swingle, Pfiffner, et al. (1933)
9. Traumatic toxemia
   - Cannon, Bayliss, and British Medical Research Committee (1918)
10. Traumatic metabolites giving capillary atony and tissue anoxia
    - Moon (1932-1938)
11. Local fluid loss
    - Phemister (1927-1930)
    - Blalock (1930)
12. Progressive oligemic anoxia
    - Harkins (1940)

This idea is supplemented by the finding in shock patients that the nerve cells of the brain show pathologic changes at necropsy. These changes were assumed to be evidence of exhaustion. This finding, upon which several books were based, in turn was founded for many years on the observations of one neuropathologic technician. Crile's first book appeared in 1899 and Lockhart Mummery (1905) agreed with the ideas of Crile on vasomotor exhaustion, with the result that in England this theory became known as the Crile-Mummery hypothesis as to the origin of shock.

Gray and Parsons (1912) recognized other factors causing nervous change, stating in this regard: "Anaemia and starvation of the central nervous system—if this is carried to a sufficient degree, the recovery of the centers is rendered impossible." These authors also found that, if a severely shocked animal was subjected to a needle puncture into the floor of the fourth ventricle, a marked rise in blood pressure occurred.

This led them to conclude that the vasomotor center is still active in the most severe degree of collapse and even in terminal states. The marked Traube-Hering waves observable in profound shock in many of their tracings corroborated this conclusion. On the basis of careful cytologic examination of animals and human beings, Gray and Parsons (1912) concluded: "Fatigue of the nerve cells does not occur in shock."

Janeway and Ewing (1914) also opposed Crile's theory, stating: "Within the time limit which we have adopted in these experiments, which is quite sufficient from the practical point of view of the operating surgeon, the exhaustion of the nerve centres by afferent stimulation of sensory nerves is a wholly negligible factor in the production of shock."

Irrespective of the merits of Crile's theory, his efforts at blocking painful stimuli went far in reducing the trauma attendant on operation. This, no matter what theory one upholds, has been shown by modern experiment to be of importance in preventing shock. Even if wrong, from the practical standpoint, the Crile-Mummery hypothesis has proved to be a useful error.

During the next few years after Crile's first publication, numerous studies were made that showed that the vasomotor center, at least, is not exhausted in shock; in fact, that it is almost overactive. The research of Porter (1907-1908) is of interest in this regard. As later quoted by Janeway and Ewing (1914): "Porter obtained in numerous experiments a greater percentage rise of blood pressure by stimulating the sciatic or vagus or splanchnic, or a greater percentage fall by stimulating a depressor nerve after the blood pressure had been reduced in shock than before the shock had been produced. . . . Nevertheless, the absolute rise or fall in Porter's experiments was very great and the experiments furnish strong evidence of the absence of fatigue in the primary stages of shock."

Just as Porter (1907-1908) claimed to show explicity that in shock the vasomotor center is not exhausted and, therefore, implicitly that the peripheral vessels are not paralyzed, so Seelig and Lyon (1909) claimed to show explicitly that the peripheral vessels are contracted and implicitly that not all the vasomotor centers can be exhausted. The classic observations of Malcolm (1893, 1905) on the constriction of peripheral vessels in shock are of great interest. Sheen (1906) tended to agree with Malcolm in a purely theoretical paper.

The article of Malcolm (1910) stands out as one years ahead of its time and deserves quotation. Malcolm discussed Crile's paper on the theory that the vasomotor centers are paralyzed in shock. He pointed out two statements in Crile's works in opposition to this conclusion. Crile asserted that both before and after death from shock "the arteries were quite empty, the tissues pale. There was a manifest transference of the blood from the arteries and the capillaries to the veins. . . . The relative

proportion of blood in the arteries and capillaries and that in the venous trunks gave a rough estimate of the depth of the shock." Crile also said that, when the splanchnic area was not involved in the manipulations of an experiment, "autopsies did not reveal a condition of vascular distension in this area different from that of other areas."

It is noteworthy that Henderson was cognizant of the lack of vasomotor collapse in shock as early as 1908, stating that the blood pressure fall in shock "is not due to abolition of the peripheral resistance in the arterial system. No inhibition or fatigue or failure of any sort occurs in the vasomotor system. On the contrary, this mechanism is intensely active in an effort to compensate the lessened blood stream."

Malcolm was also an early advocate of the importance of fluid loss being a factor in shock. He listed it more as a secondary phenomenon than as an initiating cause. As evidence for this he cited Crile's observation that saline solution was often of little value in late cases, apparently passing readily out of the veins, and pointed out that in formulating his theory, Crile "did not even mention the possibility that the fall of blood pressure might be due to a loss of fluid."

Malcolm then concluded: "A fall of carotid pressure arising from an intense vascular contraction is possible only if fluid escapes freely from the vessels into the tissues or out of the body. The chief danger of developing shock is that the tissues may be starved by arterial contraction."

Malcolm then advised against the indiscriminate use of vasoconstrictors. The remarkable thing about this work, which was well in advance of its time, is that, as Malcolm himself admitted, it was based entirely on clinical observations. Since those with whom he was arguing had performed numerous experiments, this shows once more that accurate clinical observation with carefully drawn conclusions is better than improperly controlled or incorrectly interpreted experiment.

In 1908 two prominent theories of shock appeared, the *acapnia theory* of Henderson and the *inhibition theory* of Meltzer. The research of Henderson (1908) is classic in the field of shock. He showed that acapnia will produce shock, and, while it has since been demonstrated that shock may occur without acapnia, yet these studies of Henderson contain several fundamental observations on circulatory changes in shock that represent important discoveries. The review of this theory written by Henderson in 1913 is of especial interest. Meltzer's theory can best be explained by the following direct quotations.

"In shock the activity of the functions is depressed or suspended. . . . The various injuries which are capable of bringing on shock, do so by favoring the development of the inhibitory side of all the functions of the body. . . . With regard to shock, our theory assumes that the injuries which produce shock disturb the equilibrium, causing a tendency toward

inhibition. It certainly does not mean reducing the function to a single principle, to inhibition alone; it only means shifting the tendency toward inhibition. . . . The assumpton that the insufficient activity of several functions during shock is due to a preponderating inhibitory influence refers only to the primary effect. . . . During the course of shock other influences must become secondarily active . . . anemia, asphyxia or even fatigue . . . might become operative."

The War Years, 1914 to 1918.—These years saw a continued increase in interest in shock. It is worthy of note that most of this was on the side of the allied armies. The work of Mann (1915) was the earliest on the decrease in bleeding volume (and hence, inferentially, of the blood volume). Mann showed that in a normal dog 66 per cent of the blood could be obtained from the femoral artery, while in an animal in which the viscera had been exposed until the clinical signs of shock were present, but in which the "vasomotor reflexes are as active or even more so than in the normal condition," only 28 per cent of the blood could be recovered. Shock produced by overdosage of ether or cervical cord section produced no such drop. Furthermore, Mann attributed the low blood volume and shock to a local loss of circulatory fluid.

The comment of Gatch in the discussion of this paper reveals how advanced the views of Mann were. Discussing the shock due to exposure of viscera, Gatch said: "The gist of Mann's article is that shock and hemorrhage are practically identical, that experimental shock is simply due to an extensive extravasation of the elements of blood into the peritoneal tissues, that this change is due to a traumatic inflammation and that the central nervous system has little to do with the condition."

Bloodgood in the same discussion disagreed with these conclusions, but Mann stuck to his views as shown by a later paper (1918).

Several other bits of information were obtained at this time. Guthrie (1917) demonstrated quantitatively that vasomotor tone is present in shock. Guthrie (1918) found no hemoconcentration accompanying experimental shock due to excessive nerve stimulation. The experiments of Guthrie (1918) on absence of shock following intravenous lactic acid injection tended to discount the acidosis theory. Porter (1916) emphasized the importance of observation of the diastolic pressure in determining the seriousness of shock.

Henderson, Prince, and Haggard (1917) made early observations on the metabolism of burns. They found that "the condition of shock involves a profound depression of metabolism, the oxygen consumption falling 45 per cent in one experiment and 50 per cent in another. This depression of metabolism is progressive, and ends in death."

The series of seven articles appearing in the *American Journal of Physiology* (1919) from the laboratory of Joseph Erlanger, of St. Louis, with the cooperation of Gesell, Gasser, and Meek marks an important era

in the understanding of the physiologic changes in shock. Erlanger and his associates studied shock after manipulation of the intestines, adrenalin injection, and aortic and caval occlusion. They noted that, following manipulation of the intestines, "a considerable loss of fluid from the exposed bowel occurs as a result of transudation through the serous surface, and presumably into the tissues also." Gasser, Erlanger, and Meek (1919) found that 20 per cent acacia was of benefit in experimental shock. Erlanger and Gasser (1919) showed by quantitative experiments that sodium bicarbonate injections increased the mortality following shock production. The studies of Gesell (1918, 1919) on the decrease of the volume flow of blood in shock and hemorrhage are classic. In 1918 Gesell found a marked reduction of volume flow in peripheral organs while the blood pressure was still well maintained.

At about this same time Porter (1917-1919) presented his *fat embolism theory* of the origin of shock. It is of interest that Mansell-Moullin (1894) mentioned fat embolism as a possible cause of shock.

Also at this time several important advances in treatment were introduced. The use of gum acacia was begun and blood transfusion was developed. General care was improved. The idea of Brown (1917) that, since shock is due to exhaustion, operative shock can be prevented by jejunal feeding of peptonized milk during the operation is quite out of date, despite the fact that the method may have other virtues (e.g., treatment of chronic hypoproteinemia).

The reports of the Medical Research Committee in 1919 mark an historic epoch in the study of shock. While many of these studies, performed under the exigencies and haste caused by the demands of war, were later proved inaccurate, probably more real advances and correct observations were reported in these few green-covered pamphlets than ever before or since. The work of Wallace, Dale, Laidlaw, Richards, Bayliss, Cannon, Keith, McNee, Sladden, McCartney, Telfer, Cowell, Fraser, Hooper, Drummond, Taylor, Robertson, Bazett, Bock, and Mott represents the united efforts of men from many disciplines of science to solve a gigantic problem.

A marked decrease in body temperature is often a striking feature of secondary shock. Henderson, Prince, and Haggard (1917) in a preliminary note mentioned a marked drop in metabolism in two dogs in shock. In experiments on cats under urethane anesthesia, Aub (1920) found a marked fall in the rate of basal metabolism after trauma to an extremity. The degree of fall was roughly proportional to the severity of shock produced, and recovery from shock after blood transfusion was usually associated with a prompt return of the metabolic rate to a normal level.

Aub (1920) also noted that the blood pressure change is often a late sign of shock, stating: "After muscle injury the metabolism may be

reduced before a great fall in blood pressure has occurred. . . . The *volume flow of blood* [italics Aub's] determines the oxygen delivery to the tissues, and this may vary to some degree without corresponding variation in blood pressure."

Aub (1920) reported that in animals with marked muscle trauma but without true shock only slight changes in the nonprotein nitrogen, urea, creatine, and sugar values in the blood occurred. These constituents, especially the creatine and the sugar, rose markedly as shock developed. He concluded that "the marked rise in creatine is direct evidence of the presence in the blood of products of muscle necrosis, and is therefore suggestive evidence for the theory of the chemical cause of traumatic shock."

As long ago as 1918, several French observers ascribed shock phenomenon to a liver insufficiency and Aub (1920) cited this as a possible cause for the hyperglycemia often observed. Richet and Flament (1918) noted toxic changes in the liver following shock.

Work on Shock in the Early 1920's.—Several isolated articles of interest appeared at about this time. Bock (1921) showed that, while the erythron may vary widely in medical cases, the volume of the blood plasma remains remarkably constant. The studies of Cannon and Cattell (1922) on blood pressure and the use of morphine in shock are of importance. That small hemorrhages will actually increase the plasma volume, probably because of inflow of tissue fluids, was shown by Carrier, Lee, and Whipple in 1922. A year later appeared Cannon's monograph, *Traumatic Shock*. This book summarized all the work done on shock during the War and all the output of the study stations at Dijon and Bethune. It was so complete that it seemed to close a chapter in the study of shock. In the remaining years of the 1920's relatively little was published on the subject and it remained for the 1930's to usher in the renewed interest that is to be reviewed in the present paper.

CLASSIFICATION

Classifications of shock fall into three main groups. The first is determined by origin; i.e., traumatic shock, operative shock, burn shock, obstetric shock, medical shock, etc. This is a purely descriptive differentiation. A somewhat more analytical one differentiates primary and secondary shock. Since it has been shown by Harkins (1935) and others that the changes leading to secondary shock begin as soon as the accident or other precipitating factor occurs, this classification is somewhat faulty. The so-called primary shock, then, is of two types: first, the pseudoshock state in a patient whose condition is one of uncomplicated blood pressure fall and in whom any relation to true shock is only coincidental; and second, the period in a truly shocked patient where the secondary shock state is in progress of development but is not yet obviously manifest.

TABLE II

THEORIES OF SHOCK

ROOME'S "UNIFIED THEORY OF SHOCK"

STAGE 1	STAGE 2	STAGE 3	STAGE 4
Several causes: (local loss of fluid, including hemorrhage in traumatic shock; others in other types) dehydration or starvation contributory	*Reduced circulating blood volume:* vasoconstriction by sympathico-adrenal action contributory?	*Decreased blood flow, capillary damage and increased permeability:* Pre-existing reduced flow, infection or disease, and anoxemia contributory	*Peripheral circulatory failure and death*

This second classification is faulty in the first instance in that the condition is primary, it is true, but not shock; while in the second instance it is shock but is not primary. It has served a useful purpose, however, in allowing work such as that of Blalock (1933), Roome, Keith, and Phemister (1933), and Phemister and Livingstone to differentiate between the changes occurring in the two types. It would be well to abandon the term primary shock. The word shock might well not be applied at all to the pseudoshock condition now called primary shock. "Developing" or "impending" shock would be better names for the early stages of actual shock.

The third, and possibly the best, classification of shock is that of Blalock (1934), which is as follows:

1. *Hematogenic Type (Oligemic Type).*—This comprises what is usually called secondary, traumatic, and operative or surgical shock. The essential feature is the oligemia as the initiating factor with the blood pressure fall secondary.

2. *Neurogenic Type.*—This comprises what is usually called primary shock, and its essential feature is the primary fall in blood pressure. If allowed to remain at a low level for a prolonged period, this will lead to oligemia secondarily. Shock due to spinal anesthesia or fainting is of this type.

3. *Vasogenic Type.*—Histamine shock is of this type, the action being directly on the blood vessels.

4. *Cardiogenic Type.*—In this central type of shock in contradistinction to the three previously cited types of peripheral circulatory failure, the veins are distended. This type is undoubtedly rare.

DEFINITIONS OF SHOCK

Travers (1826)	Shock is a species of functional concussion by which the influence of the brain over the organ of circulation is deranged or suspended.
Delcasse (1834)	An arrest of innervation without which all organs pass into insensibility. [An old way of expressing Meltzer's inhibition theory.]
Gross (1872)	A manifestation of a rude unhinging of the machinery of life.

Piéchaud (1880)	*Le choc est un état général plus on moins grave consécutif aux traumatismes, spécialement aux plaies par armes à feu et aux grands écrasements, caractérisé par l'affaiblissement des pulsations du coeur, l'abaissement de la tension, la pâleur des tissus, un certain degré d'anesthésie joint à la faiblesse musculaire, avec conservation de l'intelligence.*
Mansell-Moullin (1882)	A sudden check to the circulation brought about through the agency of the nervous system.
Roger (1892)	*Le choc est un état morbide qui peut se produire à la suite de fortes excitations du système nerveux et qui caractérisé par un ensemble d'actes inhibitoires dont un seul, l'ârret des échanges entre le sang et les tissus semble constant et indispensable.*
Lockhart Mummery (1905)	Surgical shock is a condition produced by exhaustion of the vasomotor centers and the resulting great fall in blood pressure.
Lockhart Mummery (1910)	A condition of lowered blood pressure resulting from exhaustion of the vasomotor centers.
Gray and Parsons (1912)	The reaction of the central nervous system to exaggerated or abnormal afferent impulses.
Morison and Hooker (1915)	A low arterial blood pressure of such duration that recovery is impossible.
Brown (1917)	Exhaustion of the food material—the Nissl granules—stored in the nerve cells, more particularly those of the vasomotor centres.
Quénu (1918)	Toxémie traumatique depressive.
Cannon (1919, 1923)	Exemia.
Meek (1926)	A decrease in the effective circulatory volume.
Schuberth (1936)	A peripheral circulatory insufficiency.
Davis (1937)	An anoxemia which is the resultant of such factors as oligemia, lowered blood pressure, diminished flow of blood, and peripheral vasoconstriction.
Tomb (1937)	The collapse of the circulation from over-stimulation of the sympathetic nervous system.
Griswold (1938)	A deficiency in circulating blood volume.
Moon (1938)	A circulatory deficiency, neither cardiac nor vasomotor in origin, characterized by decreased blood volume, decreased cardiac output (reduced volume flow) and by increased concentration of the blood.
Devine (1939)	A state of depression of all the reflex arcs accompanied by circulatory depression.
Minot and Blalock (1940)	Peripheral circulatory failure resulting from a discrepancy in the size of the vascular bed and the volume of intravascular fluid.
Selye, Dosne, Bassett, and Whittaker (1940)	A condition of suddenly developing general damage.
Freeman (1940)	The clinical condition characterized by progressive loss of circulating blood volume, brought about by the tissue anoxia which results from inadequate circulation.
Author (1940)	
Brief definition	A progressive vasoconstrictive oligemic anoxia.
Descriptive definition	An oligemia *initiated by* traumatic local fluid loss, either whole blood, plasma or both; *accompanied by* decreased cardiac output, diminished volume flow, lowered venous pressure, decreased oxygen consumption, arteriolar vasoconstriction, acapnia, and secondary blood pressure fall; and *perpetuated by* a summation of these factors and possibly hyperpotassemia, increased generalized capillary permeability, anoxia, action of tissue metabolites and deficiency of adrenal cortical hormone.

The list of definitions given above is not complete but represents a fair survey of the historical development. Mortimer (1912) criticized Gray and Parsons' definition of shock, stating that it would necessitate considering that operative shock began when the incision was made. This would seem to be unjust and the same criticism could be leveled against some of the more modern definitions. It seems logical to assume that the factors leading to shock actually begin at the time of the original injury, even if they only become manifest later.

The definitions of Cannon, Meek, Schuberth, Freeman and Griswold seem accurate. Tomb's definition is correct but may overemphasize one aspect of the question. Davis' and Moon's definitions are quite complete, and, if Moon would insert the word "progressive" before "hemoconcentration," I would agree entirely with the modified definition. My definition would apply directly only to Blalock's oligemic type and not so well to his other three types.

Shock must in nowise be confused with the so-called "shock disease" occurring in snowshoe rabbits. This disease is essentially a fatal hypoglycemia of snowshoe hares, caused by the shock of unnatural conditions, and is associated with a disturbance of carbohydrate metabolism resulting from liver degeneration.

FOREIGN LITERATURE

Short, of Bristol, England, noted as long ago as 1913 that, judging from the literature, most interest in shock was in the United States and England, and most of that in the United States. This was later true during World War I and thereafter. Parsons and Phemister (1930) noted the interesting fact that shock received relatively little attention from the Central Powers during World War I. The observation of blood pressure during operations introduced into this country by Cushing has only lately been adopted in Europe, and then to a very minor extent. In a few clinics a machine known as the *Kardiotron* keeps a record of blood pressure (Jaeger, 1937). It is quite possible that an explanation for this relative lack of interest in Continental Europe rests in the fact that the clinical men have not paid so much attention to the subject there. Irrespective of the fact that many of Crile's early ideas on shock have not stood the test of time, he served as an inspiring example to interest other surgeons in this country in the subject. Possibly that alone explains a portion of the preponderance of attention received by shock on this side of the Atlantic.

Germany.—Most of the best studies on shock are quite recent. Excellent reviews by Liebmann, of Zurich (1937), and of Eppinger (1938) on capillary permeability should be consulted. The fundamental studies of Rein (1937), of Göttingen, are especial contributions of German physiology to the shock problem. Among the German publications, those

of Ewig and Klotz (1932) are of especial importance. These authors studied the postoperative changes in blood and plasma volume by means of the CO method and hematocrit readings and found a reduction in both volumes. Studies have been made in Germany by Ewig (1938) on shock in burns, by Meessen (1938) on insulin shock, by Brüner (1938) on hemorrhagic shock, by Budelmann (1938) on "orthostatic" shock, by Schwiegk (1938) on shock accompanying pulmonary emboli, and by Hansen (1938) and Parade (1938) on obstetric shock. Other studies are considered under the appropriate heading in the present article. During the year 1938-1939, I was in Europe on a Guggenheim Fellowship to study shock experimentally and clinically. In visiting various clinics, the question of shock was usually brought up. The head of one of the largest Viennese surgical clinics was asked if he used blood or saline solution in the treatment of shock. He replied: "Never. My only treatment of shock is to elevate the foot of the bed and put novocain in the wound." This reflects the shock treatment in many European clinics, while others are quite modern.

France.—Since World War I, the subject of shock has not been studied as much in France as in this country. The work of Lambret, Driessens, Malatray, and Bizard, of Lille (1936, 1937), forms an exception to this rule. These workers have made an extensive study of the postoperative changes in blood chemistry and their relation to shock. Their observations on the decrease in blood volume attending clinical and experimental shock are quite complete. They recognized the importance of plasma loss and resultant exemia, but also considered a toxic factor due to polypeptidemia.

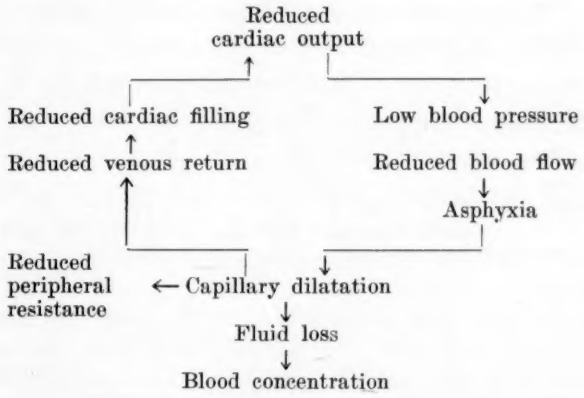
Great Britain.—The studies of Holt and Macdonald (1934), O'Shaughnessy and Slome (1935), Marriott and Kekwick (1935, 1936), Bell, Clark, and Cuthbertson (1938), Wilson and Jamieson (1938), and others are so extensive as to necessitate their being considered elsewhere in this paper. Contributions from Sweden, Russia, Italy, Spain, and other countries are also considered elsewhere.

REVIEWS

Reviews of the subject of shock include the following: 1930: Blalock; 1931: Blalock, Beard and Johnson; 1932: Rukstinat; 1933: Beard and Blalock, Blalock; 1934: Blalock, Cannon; 1935: Andrews, Dale, Frazier, Holt, Mann and Essex, O'Shaughnessy, Orr, Slome; 1936: Meek; 1937: Boyers, Clement, Tomb; 1938: Gollwitzer-Meier, Heinemann, Kirschner, Koch, Mahaffey, Roome; 1939: Allen, Cattell, et al., Cressman and Blalock, Devine, Ravdin, Rehn, Meyler; 1940: Wilson, Best and Solandt, Blalock, Harkins, Meakins, Moon, Selye, and Strumia, Wagner and Monaghan. A practical review of shock therapy was given by Fantus and Seed (1940).

The recent review of Peters (1940) very succinctly summarizes the relations of the chemical structure of the blood to surgical problems. A recent review of obstetric shock by Mathews (1939) is of interest. Important editorials on shock appeared in 1917, 1934, 1935, 1939, and 1940. Recent books entirely on shock are those of Moon (1938) and of Scudder (1940). Another book giving major emphasis to the subject is that of Blalock (1940) on *Principles of Surgical Care, Shock, and Other Problems.*

McDowall (1940) in his excellent review on shock depicted the vicious circle ("the death cycle") as follows:



Moon's Book.—This book represents such a forceful and in many ways important contribution to shock literature that it deserves a section by itself. Published in 1938, the first book on the subject in any language for fifteen years, it epitomizes the observations made by Moon and his associates at the Department of Pathology of Jefferson Medical College, Philadelphia. The title of the book, *Shock and Related Capillary Phenomena,* at once indicates the author's theory that shock *is* a capillary phenomenon.

The first portion of the book includes an excellent review of capillary structure, physiology, and pathology. This discussion leads to that of inflammation, and from here it is only a step to the exposition of the

TABLE III

SUMMARY OF EVIDENCE FOR MOON'S HYPOTHESIS: "THE WHEAL IS SHOCK IN MINIATURE"

REACTION	WHEAL	SHOCK
Capillaries	Local dilatation	Dilatation in visceral areas
Permeability	Local increase	Increased in visceral areas
Edema	Develops locally	Develops in visceral areas
Stasis	Develops locally	Develops in visceral areas
Capillary hemorrhages	Occur locally	Occur in various tissues
Perspiration	Present locally	Usually profuse

author's theory that a "wheal is shock in miniature." After a discussion of shock, the third part of the book considers various surgical and medical conditions in which a shocklike syndrome may exist. This last, again, is very instructive and valuable from a therapeutic standpoint. In fact, these two peripheral parts of the book are almost indisputable and only the ideas about shock in general are open to question.

Before passing on to a criticism of Moon's theory, it would be wise to state that theory briefly. Moon's definition of shock has already been given. If one phase of it were to be modified, it would be "characterized . . . by increased concentration of the blood." Moon, as will be discussed below, does not believe hemorrhagic shock is typical, and thus excludes it by the above statement. However, changing the word "increased" to "increasing" would allow hemorrhagic shock to be included in the definition (since after bleeding has stopped the blood tends to concentrate if shock is present). The following quotation from Moon's own summary best explains his ideas:

> The circulatory deficiencies result from a disparity between the volume of blood and the volume-capacity of the vascular system. The factors in this disparity are: (1) Those which increase the volume-capacity and (2) those which decrease the total volume of blood.
>
> The prime factor causing an *increased capacity,* is dilatation of the capillaries. A large fraction of the total capillary stream bed, which under normal conditions is closed and bloodless, is simultaneously opened to circulation. Not only is the total number of open capillaries raised above normal, their diameters are increased, thus raising their volume content.
>
> Relaxation of sympathetic nerve tonus may be a factor in the capillary dilatation. A more important factor is the direct response of the capillaries to physiologic agents, and to substances of external origin. Much has been said regarding a toxic substance originating in damaged tissues, and extensive chemical and biologic search has been made in efforts to demonstrate and identify it. These efforts have only established and confirmed the fact that in every particular its *physiologic effect* is like that of histamine. Its isolation and chemical identification have not been accomplished.
>
> In this search a consideration of highest significance apparently has been overlooked. Students of capillary physiology have shown, by evidence which has not been disputed, that metabolic substances discharged from tissue cells cause dilatation and increased permeability of the capillary endothelium with which they come in contact. These substances are liberated either by *functional activity* of the cells or by *injury* of any kind to the cells. In the one instance they initiate *functional* hyperemia, in the other, *inflammatory* hyperemia.
>
> This is a physiologic reaction and the agents which activate it should be regarded as belonging to the group of chemical messengers whose importance in the economy of the body is so immeasurable. The accumulation of these substances when the circulation of blood to a large portion of the body is obstructed, or their liberation in excessive amount following extensive injury to tissues, may produce catastrophic effects on the systemic circulation. But such effects are merely an enormous exaggeration of the normal physiologic purpose which those substances serve. To designate these substances as *toxic* requires a broad interpretation of that adjective so that it may include the exaggerated effects of hormonal substances.

Chemical investigations have not yet shown the exact composition of living cytoplasm nor of its derivatives given off during metabolic activity or released by injury. The increase in nitrogenous substances in the blood during shock suggests the presence in excessive amount, of substances derived from cells.

When an increased volume-capacity of the capillary stream bed develops, vasomotor reactions cause contraction of all the systemic arteries. The large venous channels likewise contract and the peripheral vessels become relatively bloodless. In early stages this is effective in maintaining *undiminished blood pressure,* but it is at the expense of the volume flow of blood. Stagnation and stasis develops [*sic*] in extensive capillary areas, resulting from the combined effects of their complete dilatation and of the decreased volume of fluid.

Frequently the same agent which relaxes the capillary walls renders them abnormally pervious to blood plasma. The leakage of this into the tissue spaces causes the stasis to become permanent, reduces the total blood volume, causes hemoconcentration, reduces the venous pressure and lowers the volume of venous return flow to the heart.

This type of circulatory disturbance develops in varying degrees. The capacity of the circulatory system to re-establish its physiologic equilibrium may be adequate in cases of minor severity. When the volume of blood returned from systemic areas is inadequate the arterial blood pressure declined progressively. This indicates that the mechanism of compensation is failing.

As the volume flow of blood decreases the transportation and distribution of oxygen are correspondingly reduced. The effects of anoxia are then added to the already failing circulation and the self-perpetuating vicious circle is established.

The factors which contribute to the circulatory disparity by *reducing* the *blood volume* are: loss of blood by hemorrhage, loss of plasma by leakage, and loss of fluid by perspiration, vomiting and diarrhea. Shock seen clinically or produced experimentally usually results from a combination of the factors which increase the capacity of the vascular system with those which reduce the volume of blood.

Shock is defined as a *circulatory deficiency, not cardiac nor vaso-motor in origin, characterized by a decreased volume of blood, reduced cardiac output (volume flow of blood) and by hemoconcentration.* The latter feature appears early, is easily determined and is seen in cases of moderate severity before variations in the blood pressure occur. For these reasons it is useful as an indicator. The following features are regularly associated when the syndrome is fully developed: lowered blood pressure and lowered basal metabolism, diminished renal excretion and usually an increased cardiac rate. In advanced stages the coagulability and the oxygen content of the blood are decreased, the chlorides are below normal, and both the blood sugar and the non-protein nitrogen are increased. Each of these associated features may occur in other conditions but their combination with the circulatory deficiency described completes the sydrome of shock.

A consideration of Moon's book involves two points: First, an estimate of his criticism of other theories; and second, an assay of his own. Considering the first of these, the following points stand out:

1. Moon contends that the bisection type of experiment, as used by Blalock, Phemister, and others, includes a factor of error which was not taken into account. To quote him (page 147): "As fluid escapes from the blood into the tissues of the affected side, fluid is simultaneously absorbed from the tissues of the normal side thereby decreasing its weight. Suppose 100 Gm. of fluid were so shifted: the difference

in weight of the two sides would be 200 Gm., but the *actual gain* of the affected side would be only 100 Gm. The *difference in weight* includes *twice* [italics Moon's] the volume of fluid shifted by dehydration and re-distribution, and such experiments provide no means for determining what amount of fluid is thus shifted. This factor of error, multiplied by 2, occurs in all such computations."

This contention is itself in error in two respects: First, the amount of tissue traumatized or burned is not one entire half of the body, but only about one-sixth. In fact, in Blalock's and Phemister's original experiments the weights of two opposite hind quarters, which represent about one-sixth of the body weight each, were compared. Let us suppose, as does Moon, that 100 Gm. of fluid is shifted into such a traumatized sixth and that it is absorbed from the tissues of the normal five-sixths. Twenty grams of this absorption would be from the opposite hind quarter, so the difference in weight would be 120 Gm. This factor of error of 1.2 is far from that of the 2 cited by Moon and is almost within the limits of experimental error.

Second, there is no real reason for assuming that the fluid lost one place is absorbed elsewhere. As Moon himself says, the "fluid escapes from the blood," and it is an assumption only that it is reabsorbed. Especially is this true when it is remembered that the blood volume in most experiments decreases by almost exactly the amount corresponding to the fluid lost locally, indicating that fluid is *not* "simultaneously absorbed from the tissues of the normal side thereby decreasing its weight."

2. Moon contends that shock and hemorrhage are different. He, like Coonse, Foisie, Robertson, and Aufranc (1935), makes no time classification of hemorrhage in stating this distinction. As pointed out elsewhere, Blalock (1934) showed that, while a rapid hemorrhage either produces death or recovery in most instances, a slow hemorrhage with the blood pressure kept down over a period of hours will give all the signs and symptoms of shock with the typical "wet necropsy" of Moon.

3. Moon states (page 134): "Blalock's sole criterion for shock was a decline in arterial blood pressure." This is quite untrue, as several of Blalock's publications have had as their main thesis that, except as a terminal phenomenon, certain instances of experimental shock are accompanied by practically no decline in blood pressure whatsoever.

In other places Moon criticizes details of the work of those opposing the toxic theory without giving the context of their arguments. Thus, while in certain articles the experiments reported by Blalock were all performed under barbital anesthesia, in other reports of Blalock ether and other anesthetic agents were used. Therefore, barbital could not be the cause of shock in all of Blalock's experiments as Moon tends to infer.

The second point in considering Moon's book is his own theory. Much of the evidence for a generalized fluid loss that Moon submits is qualitative. It may be true that in traumatic shock the viscera are engorged, but the important thing is the extent of the engorgement. Furthermore, many of these changes in the viscera are terminal or may be due to anoxia rather than to toxemia. Thus, cause and effect must be carefully differentiated. The views of Blalock are in contradistinction to those of Moon in this regard, as evidenced by the following quotation from the former (1931):

"The main factor which is most likely responsible for the continued low blood pressure after injuries is not a general increase in capillary permeability with loss of fluid all over the body, but a loss of blood plasma through the walls of the damaged capillaries."

Pictures presented in Slome's article (1935), comparing the histology of shock and histamine poisoning, do not agree with those of Moon (1938). Slome showed a congestive picture in histamine shock and a negative one in traumatic shock; Moon showed congestion in histamine and traumatic shock and none in hemorrhagic shock. It is probable that different time factors explained these differences, the two instances of noncongestive picture, one presented by each author, representing acute experiments where there had not been time for stasis to develop.

Then, too, Moon tries to avoid including hemorrhagic shock in his definition. This is not entirely logical and it is certain that there is no color line drawn when the fatal issue is called forth in the animal organism from fluid loss. The fact that some of the lost fluid contains red cells doesn't make it immediately less dangerous; if anything, the opposite is true. But it is just in hemorrhagic shock that the differentiation between initiating factors and perpetuating factors is most easily drawn, and, certainly, toxins or tissue products are *not* initiating factors in hemorrhagic shock. This point will be considered more fully in a separate section on the differentiation between shock and hemorrhage.

On the other hand, Moon's hypothesis explains much of the irreversibility of shock. He shows why shock is fatal and why it is a general body reaction rather than a purely local or local-brain reflex phenomenon. His book is an important landmark in the literature of shock and serves as a point of departure for much new research.

Scudder's Book.—The appearance of two books on shock (this and Moon's) within sixteen months is of interest. These two present the problem from quite different angles and it is to be noted that the second (Scudder's) hardly discusses the first at all, the approach being so different. Scudder's book contains more of an exposition of the literature, while Moon's includes a more critical review. Scudder's own thesis is based on three main points as follows:

1. "Blood studies as a guide to therapy." This sentence is a quotation from the title and indicates the importance the author places in these

observations. He makes an especial point of the use of the falling drop method. He thus makes an application of the falling drop method of Barbour and Hamilton (1926) and Kagan (1938) to the shock problem. One of the advantages of this method is that "these four tests [cell volume, specific gravity of whole blood, specific gravity of plasma, and plasma proteins] can be done in 15 minutes time" (page 68), but this statement is hard to correlate with that on the preceding page that centrifuging for an hour is necessary. Furthermore, it seems that the added benefit of this method is purely technical and the same information can be obtained in other ways (viz., Van Allen hematocrits plus direct weight method of determining specific gravity of plasma and plasma proteins, etc.). Thus, Scudder applies a new, and possibly better, method for obtaining information as to the progress of hemoconcentration. He wisely states "that shock can recur despite the correction of oligemia, emphasizes, once again, that hemoconcentration is only one of the many variable factors in shock."

It is noteworthy that Scudder does not place all the emphasis on one aspect of the blood concentration (i.e., relative proportion of cells and serum), but also considers the specific gravity of each separately and the relative protein content as well. Scudder thus considers several variables rather than one and it certainly is true that so complex a mechanism as the mammalian organism has far more than one factor upset under the stress of shock. He states that one advantage of his specific gravity method of following blood concentration is that it is accurate to 10,000 red cells per cubic millimeter; whereas, the ordinary red count is only accurate to 250,000. It is to be noted, however, that the Van Allen hematocrit gives values accurate to 1 part in 45 in a normal blood (about 100,000 red cells). Brown and Clark (1939) found that the use of a graduated pipette and direct weighing gave a more accurate index of the plasma specific gravity than the falling drop apparatus. Bailey (1939) has applied the falling drop method of determining blood concentration to cases of shock associated with nonpenetrating intra-abdominal injury. Although this writer praises the method, he gives no actual data in support of his conclusions.

2. The use of cortical extract. This will be considered under the section on that subject.

3. The increase in plasma potassium accompanying shock. This also will be considered under its appropriate heading.

An appraisal of Scudder's book is difficult until its tenets have stood the test of time. The falling drop method of studying blood concentration is certainly a technical help, even though other methods may give much the same information. The use of cortical extract has been popularized by others, especially Swingle and his co-workers (1933-1938). But the real essential feature of the book is emphasis of the

hyperpotassemia factor. The question now arises: Is hyperpotassemia one of the many *results* (or accompanying factors) of shock that on their discovery seemed so important that they were attributed as being *causes* of shock? There is a long history of such occurrences (acapnia, anoxic degeneration of nerve cells, fat embolism, low blood pressure, etc.) which have upon their discovery been graced with the title causative factor only to be later relegated to the scrap heap of results. This prompts one to consider the above question seriously. This type of reasoning, however, cannot logically exclude the fact that hyperpotassemia may be a very important causative factor in shock. The difference between *initiating* and *perpetuating* factors must also always be kept in mind.

Several of Scudder's conclusions might be worth quoting at this time (the numbers are not Scudder's):

1. Although erythrocyte counts and estimations of hemoglobin are used in measuring hemoconcentration, determination of the specific gravity of peripheral blood is superior because of its accuracy, speed, and greater sensitivity.

2. One common denominator in the phenomena of shock, whether produced by tissue abuse, loss of fluids, hemorrhage, injections of toxins, destruction of the adrenal cortex, or stimulation of the sympathetic nervous system, is a rise in plasma potassium.

3. Heat, adequate fluid administration, and the control of pain are important factors in relieving vasoconstriction, which is undoubtedly also of great importance.

4. The efficacy of transfusion in the treatment of shock is again demonstrated. Better results, however, are obtained by giving both transfusions and salt solutions, since the latter, on the basis of well-established physiologic experiments, probably is of importance in combating the underlying vasoconstriction.

5. To state that shock is due alone to potassium poisoning is fallacious. That alterations in potassium in both the blood and body fluids serve as a measure of profound cellular changes is probably more correct.

II. INITIATING FACTORS IN SHOCK

Throughout this discussion, the division into initiating, accompanying, and perpetuating factors is an arbitrary one. In each case there is considerable overlap.

1. Local Fluid Loss.—As long ago as 1913, Short stated: "The most probable cause of shock, in the writer's opinion, is oligemia, induced by loss of fluid partly into the injured area, and partly through the capillaries all over the body in consequence of reflex vasoconstriction due to stimulation of the pressor afferent nerves." Although over a quarter of a century has passed, this statement is remarkably up to

date. Short also stated that Mummery (1905), Malcolm (1905), Henderson (1908), Roy and Cobbett (no reference given), and even Sherrington and Copeman (1893) believed in transudation giving oligemia.

The classic experiment that so long prejudiced workers against the fluid loss theory can best be referred to after quoting from Cannon's original remarks (1919):

"The development of a low blood-pressure after muscle injury was proved not to be due to loss of blood from the systemic circulation, by carefully skinning the posterior extremities after death, disarticulating the legs at the knees and removing the thighs at the hip by symmetrical cuts through the tissues; the thighs were then weighed. The difference in weight was as low as 11 per cent of the estimated weight of the blood of the animal, an amount which the animal could readily lose without any fall of blood-pressure whatever."

It is to be noted that not only were the subcutaneous tissues—usually an important site of fluid loss—excluded, but also the loose regions of the groin, where most extravasated fluid migrates in such experiments. Furthermore, while the *minimum* of 11 per cent is given, no figures for the *average* are cited. It was only when these experiments were repeated by Blalock and by Phemister that a true idea of the importance of localized fluid loss in traumatic shock was shown quantitatively. This work will now be considered separately.

The Work of Blalock and of Phemister.—These two authors and their associates, working independently, are largely responsible for quantitatively showing the importance of local fluid loss in shock. A quotation from Phemister's article in 1928 is the first recorded statement based on experiment of the importance of local loss of fluid into the tissues in the production of secondary traumatic shock:

"Furthermore, necropsy examination of the traumatized limb showed increase in limb volume from hemorrhage which was sufficient to account for the fall in blood pressure. In fact, the volume of blood that it was necessary to withdraw intermittently in the course of an hour in order to kill an animal was always less than the increase in volume of the traumatized limb of the other animal, which was due very largely to hemorrhage in the tissues."

The article by Blalock (1930) entitled "Experimental Shock: The Cause of the Low Blood Pressure Produced by Muscle Injury" is certainly one of the most important papers on the subject ever written. Using a higher bisection than Cannon of *hindquarters* rather than below the groin, he found that, when one hindlimb of an animal was traumatized, there *was* enough increase in weight of the traumatized side to cause death. The old Cannon-Bayliss experiments that had concluded that there *was not* enough increase had been performed at the lower level and missed most of the edema that gravitates up into the loose tissue of

the groin. Furthermore, these old experiments were performed comparing the weights of skinned extremities and again much of the edematous tissue must have been removed in the skinning. This paper also contains the following statements that should be reread by later writers who have not correctly quoted Blalock's ideas on the identity of shock and hemorrhage. These are as follows:

"Hence, there may be two types of hemorrhage, that outside the body associated with a dilution of the blood and that into the tissues of the body associated with a concentration. . . . It is believed that these experiments indicate that determinations of the number of red cells and the amount of hemoglobin do not show whether there has or has not been hemorrhage, but rather whether the hemorrhage is outside the body or into its tissues." This last statement, especially, casts doubt on the thesis of those who put so much reliance on the presence of hemoconcentration in deciding their plan of treatment.

Johnson and Blalock (1931) made most important observations on the time relations of the blood pressure fall and the decrease in cardiac output in secondary shock (i.e., following burns, trauma to an extremity, trauma to intestines, and graded hemorrhages) and in histamine shock. The important finding was that the cardiac output dropped appreciably before the blood pressure in the secondary type of shock while the opposite situation held for histamine shock.

In studies on the effect of hemorrhage, Blalock (1934) observed that profound anesthesia by ether or barbital would give hemorrhage into the lumen of the intestinal tract and other tissue changes in control dogs. Using graded hemorrhage, the alterations in the tissues that accompany traumatic shock (the so-called "wet necropsy" of Moon) could be reproduced. Such graded hemorrhages performed under local anesthesia likewise resulted in a "wet necropsy." Blalock further found that even when local anesthesia was used, if the blood pressure was kept at a constant low level for several hours by graded hemorrhages alternating with introduction of more blood, "death occurred in all the experiments, despite the fact that more blood was introduced than was removed." Brooks and Blalock (1934) made observations quite similar to these. In agreement with Blalock (1927), Swingle, Pfiffner, Vars and Parkins observed (1934) that the slower the bleeding, the greater the quantity of blood which can be removed without symptoms of shock appearing.

In an article appearing two months after Blalock's, Parsons and Phemister (1930) reported work done independently that reached the same conclusions as had Blalock (1930). Also using a higher amputation than Bayliss and Cannon (1919), Parsons and Phemister found that a traumatized limb of a dog is heavier than the corresponding untraumatized limb to an appreciable degree. This increase in weight was considered to be the "predominating factor in the production of the circulatory failure."

This article by Parsons and Phemister and that by Roome, Keith and Phemister (1933) on the effect of bleeding after reduction of the blood pressure by various methods are classics in the study of shock. In the second article it was reported that the bleeding volume, as shown in Table IV, was only slightly reduced in shock due to hyperventilation, anaphylaxis, histamine administration, spinal cord section, and spinal anesthesia. In another type of shock the reduction was marked; namely, following trauma to an extremity, hemorrhage, plasmapheresis, and intestinal manipulation. The shock present in this second type with lowered bleeding volume is what is usually known as secondary shock.

TABLE IV

BLEEDING VOLUME IN VARIOUS TYPES OF SHOCK*

ADOPTED FROM ROOME, KEITH, AND PHEMISTER (1933)

SERIES	PROCEDURE	NO. OF CASES	AVERAGE BLEEDING VOLUME, PER CENT OF CALCULATED BLOOD VOLUME	AVERAGE OF GROUP
1.	Normal dogs	20	58.6	58.6 (Normal)
2.	Hyperventilation	5	56.2	
3.	Anaphylaxis	5	51.0	
4.	Histamine administration	6	50.5	
5.	Spinal cord section	6	48.0	
6.	Spinal anesthesia	6	44.0	49.9 (Primary type of shock)
7.	Trauma to an extremity	4	24.6	
8.	Hemorrhage	7	24.9	
9.	Plasmapheresis	5	19.7	
10.	Intestinal manipulation	6	18.0	21.8 (Secondary type of shock)

*The bleeding volume is the amount of blood that can be removed after maintaining the blood pressure at a low level by the procedure in question.

Freedlander and Lenhart (1932), by means of standardized trauma to the limbs of cats, confirmed the work of Parsons and Phemister (1930) and of Blalock (1930). In addition, they believed they were able to exclude the possibility of nervous factors. Likewise they compared the amount of blood that could be bled from control cats and found it similar to the amount of extravasation in the traumatized cats. The work of Herbst (1933) on rabbits comes to essentially the same conclusions, although in a later paper (1934) Herbst tends to emphasize nervous factors.

The paper of Phemister and Livingstone (1934) expresses views on primary shock similar to those of Blalock (1934). Emphasizing that "primary and secondary shock should be recognized on the basis of difference in etiology rather than difference in time of occurrence," they point out that most cases of low blood pressure resulting from painful or frightening procedures or from major operations under anesthesia

may be classed as psychogenic or neurogenic in origin. These reactions are essentially reversible and of minor importance.

Beard and Blalock (1931) studied the composition of the fluid that escapes from the blood stream after mild trauma to an extremity, after trauma to the intestines, and after burns. They found the fluid to be comparable to plasma in chloride, sugar, and nonprotein nitrogen and the fluid protein value to be about 80 per cent that of the corresponding plasma. They concluded: "It is believed that the results of these experiments indicate that the loss of plasma proteins is the most important factor in the production of the low blood pressure after the procedures reported." Certainly, this is an important observation, for the mammalian organism can far less easily lose plasma than plain water. Blalock (1934) studied the influence of exposure to cold and of deprivation of food and water on the development of shock. He found that the latter two items had little effect on the resistance to hemorrhage and trauma. However, exposure to cold had a profound influence, depending especially on its duration and the depth of anesthesia.

In secondary shock Blalock (1933) reported a decrease in cardiac output before the blood pressure began to fall. In contradistinction to these results he found that primary shock (the immediate decline following striking the abdomens of anesthetized dogs) was accompanied by an increase in the cardiac output in seven of ten experiments. Furthermore, the oxygen consumption increased during and immediately following the traumatization in nine of ten experiments.

When milder and nonfatal trauma was given in sixteen anesthetized dogs, Blalock (1931) found that the decrease in blood pressure was roughly proportional to the loss of plasma, as evidenced by the difference in weight of the traumatized and the opposite normal limb. Thus:

5 experiments, final mean blood pressure 108 mm. Hg
Difference in weight of limbs averaged 2.41 per cent body weight
10 experiments, final mean blood pressure less than 70 mm. Hg
Difference in weight of limbs averaged 3.66 per cent body weight

Harris and Blalock (1931) found that over a period of hours the muscles of dogs anesthetized with barbital became more dehydrated than experimental animals submitted to trauma under the same anesthesia, although in all cases a slight dehydrating effect occurred. Other contributions of Blalock and of Phemister are considered under their appropriate headings.

Freedlander and Lenhart (1932), as already stated, performed experiments quite similar to those of Parsons and Phemister (1930) and of Blalock (1930). These later experiments compared the shock resulting from trauma to normal cats and to cats with completely denervated limbs. The two series responded in a like manner to the trauma. Furthermore, the amount of fluid and blood recovered in the traumatized

limbs was quite similar in amount to that which produced death of other cats by bleeding. After excluding nervous factors, Freedlander and Lenhart concluded: "The shock following trauma can be explained on the basis of hemorrhage and local fluid loss."

Holt and Macdonald (1934), of Manchester, repeated the work of Phemister and Blalock with confirmatory results. They first did experiments with the blood returning from traumatized limbs and found on reinjection that the blood always gave a pressor rather than a depressor response. Then in a series of ten dogs with trauma to one extremity and comparison of the weights of the normal and traumatized limbs, they found the relative increase in weight of the traumatized side to equal 57 per cent of the calculated blood volume (a range of 30 to 83 per cent). This value checks quite closely with those of Blalock and of Phemister. Holt and Macdonald also found that shock developed in other animals following trauma just as readily when the nerve impulses were cut off by spinal anesthesia or when toxin absorption was prevented by common iliac vein occlusion.

The important question arises as to the amount of fluid which, when lost from the blood stream, will produce death. Experimental reports differ somewhat on this score. Boyce, Lampert, and McFetridge (1935) reported that dogs could be bled 4.6 per cent body weight without shock or death resulting. Roome, Keith, and Phemister (1933) reported that 4.5 per cent blood loss would produce death in dogs, and Johnson and Blalock (1931) found the same figure to be 5.1 per cent. Elman and Cole (1934) found that death followed a 2.7 per cent loss of blood from hemorrhage in normal cats. Older observations on the extent of fatal hemorrhage in dogs include those of Béchamp (3 or 4 per cent body weight) and Huenerfauth (3.5 to 4.5 per cent body weight). Evidence obtained from plasmapheresis experiments indicates that experimental animals cannot tolerate the loss of plasma as well as whole blood. These latter experiments are open to the objection that the reinjection of centrifuged cells after the removal of plasma may introduce factors that must be reckoned with besides the plasma loss. The centrifuged cells, even if not hemolyzed, may hasten the occurrence of death in an already weakened animal. Johnson and Blalock (1931) found that dogs would die after loss of varying amounts of blood plasma by plasmapheresis, dependent on the time interval. When the blood plasma was removed in amounts equalling 0.5 per cent weight at hourly intervals, the total amount removed in percentages of body weight varied from 2.5 per cent plasma and 1 per cent whole blood to 3.5 per cent plasma and 0.85 per cent whole blood. The average sum of these figures was 4.05 per cent, which was the average total loss of plasma and whole blood. The figure for the whole blood is necessarily included, because the animals died before the red blood cells from the last bleeding had been replaced.

The average increase in hemoglobin was 34 per cent of the control figures. When the bleedings were performed at six-hour intervals, the average loss was 2.4 per cent plasma and 0.2 per cent whole blood. The sum of these figures is 2.6 per cent, which was the average total loss of plasma and whole blood. The average increase in hemoglobin was 24 per cent of the control figures. Roome, Keith, and Phemister (1933) found that an average plasma loss of 3 per cent body weight in a series of five dogs would reduce the blood pressure to a shock level. These authors found the terminal blood loss in this series to be 1.4 per cent body weight. This makes the total plasma and blood loss 4.4 per cent. The blood was concentrated by this procedure, but no figures in this regard are given in this report. The authors state that removal of less plasma than whole blood would produce death.

Harkins and Harmon (1937) did additional plasmapheresis experiments as shown in Table V, and found that the average amount of plasma which, when removed from experimental animals, will produce death, was 4 per cent body weight. It is noted from the table that the final blood pressure and extent of the hemoglobin and hematocrit rise, as well as the duration of the procedure, are all quite comparable to those occurring in other acute shock experiments.

There seems to be, then, considerable evidence for the importance of local fluid loss being a significant initiating factor in the causation of shock. Robinson and Parsons (1931) have written concerning this concept. Frank (1938) is for local fluid loss and against nervous factors being the cause of shock. Much of the criticism of this theory is based on the misunderstanding that it should explain the whole course of a shock case. Because the diphtheria bacilli do not directly cause terminal myocarditis or tracheal obstruction, we do not argue that they are not the cause of the disease. Similarly, in shock, because a dying patient develops capillary congestion, increased capillary permeability, and breakdown of cell membranes with discharge of cell potassium, this does not argue that the original fluid loss, which precipitated these changes, was not the cause. However, to say that local fluid loss is the only cause or that it acts equally in all types of shock is like riding a good horse to death.

2. Should Shock Be Differentiated From Hemorrhage?—Blum (1876) stated that shock is hemorrhage and hemorrhage is shock, and this idea has been popular with some other authors since that time. The association of the two conditions, shock and hemorrhage, in practice is epitomized by the introductory sentence of an article by Erlanger and Gasser (1919): "The injuries that lead to shock in man almost always are accompanied by more or less hemorrhage."

On the other hand, Moon in his book (1938), as already stated above, tries to differentiate between shock and hemorrhage. This idea was

TABLE V

RESULTS OF PLASMA REMOVAL IN EIGHT ANIMALS

In Most Instances the Final Blood Pressure, Hemoglobin, and Hematocrit Readings Were Taken Just Before the Final Bleeding

EXP. NO.	BLOOD PRESSURE		HEMOGLOBIN		HEMATOCRIT		DOG WEIGHT KG.	NO. OF BLEEDINGS	INTERVALS IN HOURS FROM FIRST TO LAST BLEEDING	PLASMA REMOVAL PER CENT BODY WEIGHT	BLOOD REMOVED TERMINALLY PER CENT BODY WEIGHT	TOTAL AMOUNT PLASMA PLUS BLOOD REMOVED TERMINALLY PER CENT BODY WEIGHT
	INITIAL	FINAL	INITIAL	FINAL	INITIAL	FINAL						
1	150	56	100	145	53	69	9.3	6	4	3.5	0.0*	3.5
2	120	60	89	148	45	68	9.8	7	·9	4.2	0.0	4.2
3	156	70	102	152	44	64	10.4	3	7	3.0	0.8	3.8
4	148	40	77	121	33	56	15.4	7	4½	4.5	0.4	4.9
5	140	48	92	130	62	72	27.0	7	20	3.8	0.5	4.3
6	152	44	92	142	47	66	19.0	7	10	5.6	0.0	5.6
7	146	78	106	168	49	75	13.0	10	10	4.6	0.0	4.6
8	140	68	101	167	57	81	21.5	9	19½	2.8	1.1	3.9
Average	144	58	95	147	49	69	15.8	7	10½	4.0	0.4	4.4

*In the experiments in which no blood was removed terminally, death occurred between bleedings and after the final red cell reinjection.

previously presented by Moon and Kennedy (1932) and since has been presented by Moon in a separate article in the *Annals of Surgery* (1939).

Coonse and associates (1935), next to Moon, have been the most ardent recent proponents of the tenet that shock and hemorrhage are different. They stated that traumatic shock is accompanied by acidosis and increased blood concentration, while hemorrhagic shock is not. It is quite true that hemorrhage of sudden onset will have no acidosis immediately, but once depleted of blood the experimental animal will soon develop acidosis. Furthermore, if the hemorrhage is completely arrested, the blood thereafter may become concentrated just as in other shock, especially if the blood loss has been gradual. Later, Coonse and his coworkers admitted that slow hemorrhage simulates traumatic shock. These authors also stated: "Hemolysis has been shown to be consistently present in traumatic shock." "In slow hemorrhage, the findings more nearly resemble those of traumatic shock."

Other authors also try to differentiate shock from hemorrhage. Thus, Mahaffey (1938) listed symptoms diagnostic of hemorrhage—restlessness, anxiety, thirst, and nausea—which are generally recognized as applying equally well to shock. He further stated:

"In hemorrhage, we have a loss of whole blood together with a diminution of the red cell count. In traumatic shock, we have a loss of blood plasma into the injured tissues with a concentration of red blood cells in the circulation."

Hendon (1938) also attempted to differentiate the two, stating: "We do things for shock that we would not do for hemorrhage." He recognized, however, that the two conditions often occur simultaneously. Archibald (1934) also stated in a purely clinical article: "Hemorrhage has nothing to do with pure traumatic shock." This seems to be a rather extreme statement. Furthermore, the remark of Moon that trauma-to-limb experiments are really nothing but instances of hemorrhage is controverted by the fact that Blalock found the hemoglobin content of the fluid expressed from the limb to be only 30 per cent of that obtained from the control. Woodhouse (1940) claimed that bleeding following ruptured ectopic pregnancy is often associated with a slight fever (2 to 2.5°), while shock is not accompanied by fever. This may apply in some cases to hemorrhage into the peritoneal cavity, but certainly not to external bleeding and only occasionally to bleeding into the tissues. An increase in the blood lactic acid after hemorrhage is reported by Riegel (1927). Foote and Gerst (1940) have applied the use of combined specific gravity readings by the falling drop method on whole blood and plasma in the treatment and differentiation of shock and hemorrhage. Leucocytosis in shock and hemorrhage was made the subject of a recent editorial (1940).

Probably the best contradiction of the ideas of Coonse and associates (1935) and Moon (1938) that shock and hemorrhage have little in common and that in the latter there is no general escape of fluids from the blood stream is that of Blalock. This author (1934) pointed out that such a general loss takes place when the blood pressure remains at a low level for several hours. "One rarely encounters in patients, as a result of hemorrhage, a low blood pressure for an extended time. When hemorrhage from a large blood-vessel takes place, usually either the patient dies almost immediately or the remaining volume of blood is augmented by natural or artificial means and the blood-pressure rises." Freeman (1935) also disagreed with Moon and Kennedy's (1932) differentiation of shock from hemorrhage and pointed out again that they did not adequately consider the time factor in hemorrhage experiments.

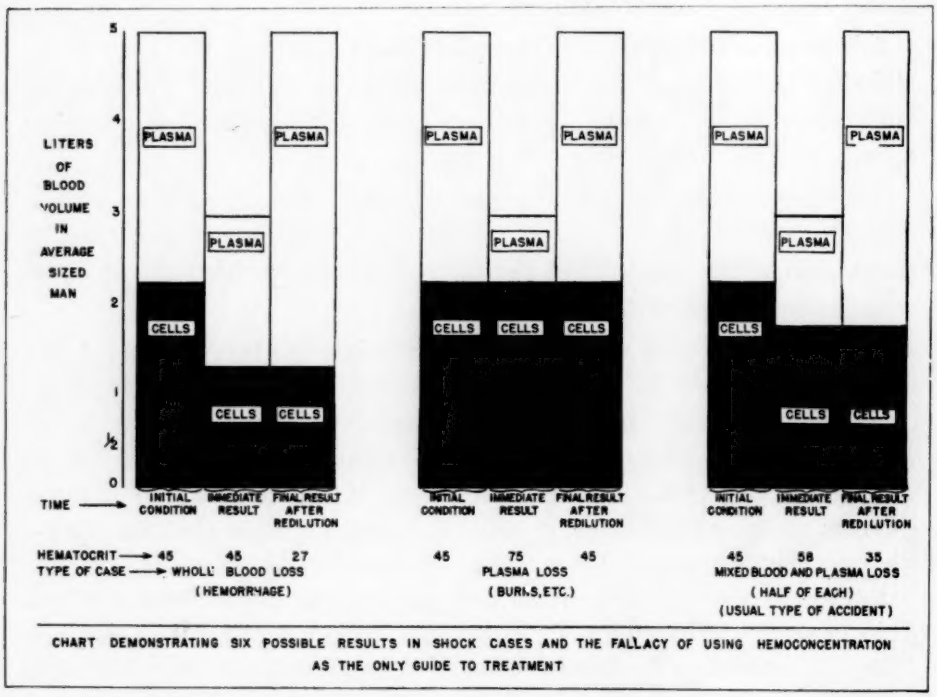


Fig. 1.—Hemoconcentration and shock. This figure demonstrates the variability of the relation between the two.

In experiments on shock produced in two ways, (1) repeated trauma to both hindlimbs and (2) repeated hemorrhage, Davis (1937) attempted to show if shock produced by trauma was similar to that produced by hemorrhage as evidenced by the histopathologic changes. The results indicated no essential difference. In both instances there was a variable amount of blood-stained, plasmalike peritoneal fluid, the intestines were relaxed and flabby, and constriction of the arteries was present. No

evidences of splanchnic congestion were found. The lungs were edematous to a degree, depending on the duration of the shock state, and the heart was diminished in size proportional to the decrease in blood volume at the time of death. Davis concluded: "It may be stated that the histopathologic appearance is the same both in traumatic and hemorrhagic shock, which suggests that the basic etiology is similar."

It would seem that from the practical standpoint alone, a differentiation between hemorrhagic and other types of shock is disadvantageous. In clinical cases usually both whole blood and plasma are lost. A patient suffering from shock, who has lost a little whole blood in addition, is just as deserving of shock treatment as a simpler case. After all, it matters little what color fluid is lost from the blood stream, red or yellow. The numerous possible combinations of blood concentration after complicated injuries are shown in Fig. 1.

III. ACCOMPANYING FACTORS IN SHOCK

A number of changes occur in shock that are common to most types. Many of these may be initiating or perpetuating factors as well, but at least their presence is common and they are present through most of the course of shock. Hence, they will be considered at this point. Reference should be made to Table VI. If the causal relation is to be emphasized,

TABLE VI

HISTORICAL DEVELOPMENT OF EVIDENCE FOR CERTAIN FEATURES OF SHOCK*

1. *Oligemia*
   - Short, 1913
   - Mann, 1915
   - Robertson and Bock, 1918
   - Keith, 1919
   - Gasser, Erlanger, and Meek, 1919
   - Gesell, 1919
   - Phemister, 1930
   - Blalock, 1930
   - Freedlander and Lenhart, 1932
   - Holt and Macdonald, 1934
   - O'Shaughnessy and Slome, 1935

2. *Decreased cardiac output*
   - Boise, 1907
   - Henderson, 1908
   - Markwalder and Starling, 1913-1914
   - Wiggers, 1918
   - Blalock, 1931

3. *Vasoconstriction*
   - Lister, 1858
   - Mapother, 1879
   - Malcolm, 1893
   - Sheen, 1906
   - Gray and Parsons, 1912
   - Short, 1913
   - Pilcher and Sollmann, 1914
   - Freeman, 1935

4. *Vasomotor center intact*
   - Porter, 1907-1908
   - Seelig and Lyon, 1910
   - Mann, 1914
   - Wiggers, 1914
   - Pilcher and Sollmann, 1914
   - Cattell, 1922

5. *Decreased blood flow*
   - Morison and Hooker, 1915
   - Gesell, 1917-1918
   - Erlanger and Gasser, 1919
   - Aub and Cunningham, 1920
   - Freeman, 1935

*These lists are not exhaustive.

these factors might be called "sustaining factors" as well as "accompanying factors."

1. *Oligemia.*—This is undoubtedly one of the most important changes occurring in shock. Erlanger, Gesell, and Gasser (1919) had early demonstrated an increase in the peripheral vascular tone in experimental shock. Gesell (1919) found that a decrease in blood volume of less than 10 per cent produced by hemorrhage may cause a decreased blood flow through the submaxillary gland of more than 60 per cent even though accompanied by a rise in general arterial blood pressure. Roome, Keith, and Phemister (1933) noted a low "bleeding volume" in hemorrhagic and traumatic shock and a near normal one in histamine shock. Using the carbon monoxide method, Aikawa (1935) found the decrease in blood volume accompanying surgical operations on dogs to average 18 per cent with many values showing more than 30 per cent decrease. Since many of these operations were minor, the decrease in shock-producing procedures should average considerably more. Derra (1937) showed a reduction in blood volume accompanying anesthesia.

Derra (1936) used a combination of the carbon monoxide and dye methods in studying blood volume changes in dogs under avertin anesthesia and observed both increases and decreases, the range being from plus 45 per cent to minus 28 per cent of the preoperative values. He observed that during laparotomies the plasma volume tended to fall and the cell volume to rise with decrease in the total volume. More recently Gibson and Branch (1937), of Boston, did blood volume studies on twelve surgical patients by the Evans blue dye method. They found that the total volume is reduced at the end of the operation, the reduction being due to a diminution of plasma volume larger than can be offset by influx of red cells into the circulation. None of their patients were in a condition of shock, the blood pressure being well maintained throughout, and apparently no great external loss of blood occurred. Neuwelt (1939) found the vital red dye method for determining blood volume accurate for normal dogs but inaccurate in dogs in shock. He also found that splenectomy produces a decrease in circulating blood volume and that such animals develop shock more easily than normal dogs.

The new studies of Gibson and Evans (1937), Gibson and Branch (1937), Gibson, Keeley, and Pijoan (1938), Gibson and Evelyn (1938), Gregersen, McAllister, Pinkston, and their associates (1935-1938), and Gregersen and Stewart (1939) on blood volume by means of the use of the Evans blue dye (T-1824) have opened up a new field. This method, using either a spectrophotometer or photoelectric colorimeter, has made the determination of blood volume much more accurate than any previous method. This new procedure has once again confirmed the observation that oligemia accompanies shock.

2. *Diminished Blood Flow.*—It is a common observation in both patients and experimental animals with shock that the peripheral blood flow is decreased. Thus, there is great difficulty in obtaining (or administering, because of difficulty in doing a venipuncture) blood from superficial veins or from ear or finger punctures in severe shock. More quantitative evidence of this decrease in peripheral blood flow was obtained by Freeman, Shaw, and Snyder (1936), who found that the blood flow through the hand is markedly reduced in shock patients.

The importance of reduction of blood flow was early recognized by Gesell and Moyle (1922), who found a decrease in the volume flow of blood through the striated muscle of dogs after hemorrhage. In a series of hemorrhages in the same animal, the late ones invariably produced the greatest reduction in blood flow. Injections of gum saline solution produced an increase in volume flow out of proportion to the increase in blood volume. In a later paper (1922) these authors reported a decreased response to electrical stimuli associated with the decreased volume flow in muscles. They discussed the relation of this change to nutrition of the tissues and in turn the role played by these factors in shock.

More recent observations on this point include those of Meek (1936), Freeman, Shaffer, Schecter, and Holling (1938), Roome (1938, 1939), and others. Klemperer, Penner, and Bernheim (1940) believe that the intestinal lesions present in shock are due to spasm of the vessels. Further studies on the general subject of blood flow through the dog's paw were made by Freeman and Zeller (1937). Cammer and Griffith (1939) showed that the intra-arterial injection of adrenalin reduces the blood flow and O_2 consumption of the intact hindlimb of the cat. The recent observations of Roome (1938) on the effect of intra-arterial epinephrine on the blood flow in an extremity are of great fundamental importance. This author, using his own photoelectric modification of the Ludwig Stromuhr, injected small doses of epinephrine into the femoral artery of dogs. The typical response seemed to be a dilatation of the capillaries and a constriction of the arterioles and arteries in the muscles. Roome (1939) found a marked diminution in the peripheral blood flow to occur in dogs with only moderate hemorrhage. He concluded that this lent "support to the ischemic theory of shock."

Blalock and Levy (1937) studied the blood flow through the posterior part of the body, the kidneys, the portal system, and the anterior extremities and head before and after (a) hemorrhage, (b) intestinal trauma, and (c) histamine administration. Hemorrhage and intestinal trauma were accompanied by a greater diminution in the flow of blood through the posterior part of the body and a smaller decrease elsewhere. Histamine, on the other hand, was usually associated with a general reduction in the flow of blood throughout the body. This once

again confirms the opinion that histamine and traumatic shock are different. It is to be remembered that Johnson and Blalock (1931) showed that in hemorrhagic and traumatic shock the cardiac output declines first; whereas, in histamine shock the blood pressure falls first.

All of these writers obtained confirmatory results and it seems to be without question that a decrease in blood flow is one of the prime factors in shock. So important and progressive is it that one might almost say that to diagnose shock a lancet to cut the ear or finger and determine the blood flow would prove almost as useful as all the sphygmomanometers ever made. If one were to select a single determination to follow the course of shock, an observation of the peripheral blood flow might be the best to choose.

3. *Inadequacy of Fall in Blood Pressure in the Diagnosis of Shock.*—It has already been mentioned that in secondary shock a fall in blood pressure is often a terminal phenomenon occurring long after marked hemoconcentration and decreased blood flow have become evident. We have indeed come a long way from the belief implied in the statement of Rowell speaking before the annual meeting of the British Medical Association in 1910 that: "A falling blood pressure is the first sign of the onset of shock." A more modern opinion is that expressed by Blalock (1927): "The blood pressure is an inadequate guide to the state of the circulation in incipient shock."

Older observers had noted that there were marked changes in the circulation before a shock level of blood pressure was approached. Gesell (1919) showed a slowing of blood flow through the salivary gland before a fall in pressure occurred. Henderson (1909), in working on shock produced by intestinal trauma in dogs, found a markedly decreased oxygen content of venous blood. In severe anemia the oxygen content of venous blood may be as low as in shock, but that of arterial blood is likewise reduced as shown by Aub (1920). The conclusions of this latter author are worth listing:

1. There is a markedly diminished oxygen content of the venous blood in experimental traumatic shock. This change occurs before the blood pressure falls to a shock level and is still present after apparent recovery from shock.

2. The blood flow is also greatly decreased in the development of, during, and after shock.

3. The resulting anoxemia of the tissues may be the cause of the decreased metabolism.

4. *Acapnia.*—The idea that the acapnia which accompanies shock might be a causative factor was introduced by Henderson (1908). This was partly based on experiments on the production of shock by overbreathing alone. Janeway and Ewing (1914) showed that, while artificial respiration when rapidly given leads to acapnia and shock,

when carbon dioxide is given at the same time and there is no acapnia, shock develops anyway. These authors believed that this shock was the result of increased intrabronchial pressure and not of acapnia. It thus seems that acapnia is a result rather than a cause in most types of shock. Milroy (1917) showed that there is a low alkali reserve after hemorrhage. Further observations on acapnia and blood volume were made by Henderson (1930) and Rühl (1938). Seevers and associates (1939) presented data which, when compared with the effects of voluntary hyperpnea in man and correlated with the results of animal

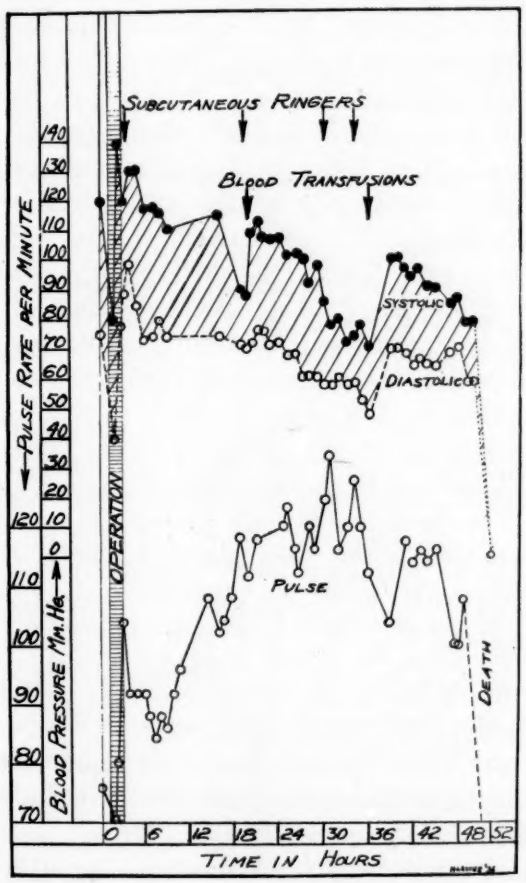


Fig. 2.—Inadequacy of observation of fall in blood pressure in diagnosis of shock due to hemorrhage. In this patient with malignancy of the head of the pancreas, marked jaundice, and postoperative bleeding into the peritoneal cavity, treated before the days of vitamin K, it is seen that the fall in blood pressure was not a perfect guide as to the seriousness of the condition until shortly before death. The increase in pulse rate was a much better guide early, but its late improvement was deceiving.

experiments, show that the arterial hypotension due to the rapid removal of carbon dioxide is a phenomenon which obtains only during anesthesia. They believe it is incorrect to classify this hypotension as surgical shock, since (1) the hypotension is not progressive, (2) recovery of arterial pressure occurs even during continued ventilation, and (3) when hyperventilation is discontinued, recovery is immediate.

Associated with or related to the acapnia is often an *acidosis.* Hertzman and Gesell (1926) showed that following hemorrhage there is an increased acidity of the venous blood. Because of this acidosis, Cannon (1918), Coonse and co-workers (1935), and others advised intravenous sodium bicarbonate in shock cases. It now seems that acidosis is not a causative factor in shock and there is no basis for treating it at present. The underlying anoxia is probably much more important.

5. *Decreased Muscle Tonus.*—The possibility that muscle tonus may be of importance in helping the venous return of blood to the heart, and hence in maintaining an adequate cardiac output, has been discussed by Henderson (1931, 1938, 1939), Henderson, Oughterson, Greenberg, and Searle (1934, 1936) and Beigelböck and Steinlechner (1938). Ornstein, Licht, and Herman (1939) have suggested that, if low muscle tonus is a factor in shock, faradic stimulation of muscles might be of help. They found that such stimulation increases the muscle tonus and at the same time raises the venous pressure.

6. *Decrease in Venous Pressure.*—Certain older writers, including Crile (1899), Sheen (1906), and Penfield (1919), reported an elevated venous pressure in shock. Possibly because certain of their readings were made in the portal system these results are not in agreement with modern studies which show almost unanimously that the general venous pressure is decreased in shock. They include the observations of Morison and Hooker (1915), Wiggers (1918), Henderson (1931), and Ornstein, Licht, and Herman (1939). Wiggers (1918) stated in this regard: "The decreased venous pressure and consequent reduction in minute output is the predominate factor in the pronounced fall of arterial pressure during the progressive stage of shock." His next statement in the same article would not bear up so well under modern scrutiny, however, if the work of Freeman (1933), is to be considered, for Wiggers attributed the initiating factor to be a "reduction in peripheral arterial resistance."

Other important accompanying factors in shock are merely listed here because they are discussed elsewhere in this paper. In many cases these are of just as much or more importance as those more fully discussed above, and the discrimination is in other ways entirely arbitrary.

7. *Hemoconcentration* (see Initiating Factors).
8. *Decreased Cardiac Output* (see Initiating Factors).
9. *Vasoconstriction* (see Adrenal Medulla).
10. *Decreased Metabolism* (see Anoxia).
11. *Capillary Congestion* (see Histamine).

Miscellaneous Experimental Studies.—Many of these, having important bearing on the shock problem as a whole, are presented here, rather than under separate headings as are other studies. The fundamental work of Swindle, of Milwaukee (1936), on the perivascular

seep valves and their relation to the exchange of body fluids has an important bearing on this aspect of the shock problem. The work done in Krogh and Rehberg's laboratory by Asmussen, Christensen, and Nielson (1939) on the relation of posture to circulation has an affiliation to the shock problem. Other interesting studies include those of Fåhraeus (1931), who showed that below a critical point of about 0.3 mm. for the diameter of a tube blood does not obey the law of Poiseuille, but actually has less viscosity than would be so if it were a homogeneous liquid. These studies have an applicability to the flow of blood in arterioles in shock.

The studies of Adolph, Gerbasi, and Lepore (1933, 1934) on fluid redistribution after hemorrhage and transfusion are of interest. They found that the dilution of the plasma following hemorrhage, and presumably due to influx of tissue fluids, requires about twenty-two minutes for its approximate completion. Following transfusions and other infusions, the redistribution of fluid was also quite rapid. Davis and Jermstad (1939) performed experiments to study the regional redistribution of blood in experimental secondary shock. Anesthetized animals were placed on a platform and the relative weights of the head, thoracic, splanchnic, and hindlimb regions determined serially. There was a similarity in the regional redistribution of blood after hemorrhage and that after trauma. A shift from the splanchnic area occurred with early increase in the blood in the thoracic area followed by a decrease. A late increase in the blood in the extremity areas occurred. The authors concluded from this experiment, which is rather elaborate and technically difficult to interpret, that "direct experimental evidence is offered against the occurrence of a splanchnic 'pooling' of blood in traumatic and hemorrhagic shock."

Davis (1937) performed another interesting series of experiments to test the theory of "splanchnic pooling" of blood in shock. These experiments attempted to determine quantitatively the regional redistribution of blood in the intact animal in a state of shock. By the use of a specially designed apparatus, the head, thoracic, abdominal, and peripheral (hindlimb) areas of nembutalized dogs were weighed before and during the production of secondary shock. It was found that trauma is associated with a loss of bloody fluid into the traumatized area. Simultaneously blood is lost from the cephalic, splanchnic, and thoracic regions, except in very long experiments where a secondary increase in weight of the thoracic area takes place as a result of edema of the lungs. In hemorrhagic shock the greatest loss is from the splanchnic area and to a lesser extent from the thoracic and cephalic regions. In histamine shock blood is shifted into the thoracic and abdominal areas. These findings do not provide any evidence for

splanchnic pooling in traumatic or hemorrhagic shock but furnish differentiation of histamine shock from shock of traumatic or hemorrhagic origin.

The experiments of Doménech-Alsina and his associates of Barcelona (1933) are of great interest. These experiments revealed that shock could be produced by irrigating the peritoneal cavity with hypertonic solutions. The following irrigations were performed:

1. Hypertonic saline solution (40:1,000) gave a progressive blood pressure fall, with a decrease in the carbon dioxide reserve and an increase in the hemoglobin and chlorides in the blood. Sometimes the blood pressure fell suddenly at the end of the experiment after being relatively well maintained hitherto.

2. Isotonic saline solution (7:1,000) gave no blood pressure change or slight fall, no change in hemoglobin or chlorides, decrease in carbon dioxide reserve.

3. Hypotonic saline solution (3:1,000) gave no change in blood pressure or carbon dioxide reserve, slight increase in hemoglobin, decrease in chlorides and glucose.

In these experiments it was found that adrenalectomized dogs died more quickly than the control animals. Experiments somewhat similar to those of Doménech-Alsina were performed by Curtis and by Davis, Hanke, and Curtis (1930). These authors perfused the peritoneal cavity of rabbits with distilled water and produced a marked hypochloremia. The experiments of Curtis and Huggins (1928) indicate that even normal saline solution will irritate the peritoneum of rabbits.

IV. IRREVERSIBILITY OF THE SHOCK SYNDROME

One of the most interesting features of shock is that after it has existed a certain time measures that would have led to recovery in the early stages are of no avail. This irreversibility exists in shock due to trauma, burns, and other injuries. The experiments of Pilcher and Sollmann (1914) indicate that shock from hemorrhage is also irreversible. These authors found that as dogs are bled, if the blood is reinjected during an early stage of the process, recovery is possible, but later blood pressure "can only be brought back to 60 mm., no matter how much fluid is injected." Blalock (1934) came to similar conclusions with regard to hemorrhage.

Cannon (1919) gave a discussion of the vicious circles in shock. Fantus (1938) is another who recognized the irreversibility of the shock syndrome. While shock is undoubtedly irreversible in its later stages, it is not so much so as inferred by O'Shaughnessy and Slome's statement (1935) as follows: "It has been our experience that the subject of severe trauma who does not show some signs of recovery under established modes of treatment within two or three hours of his injury is almost inevitably doomed." A case of mine[388] is at least one

exception to this rule. This may, however, merely be another bit of evidence for the fallibility of blood pressure readings in shock prognosis.

As to the cause of the irreversibility in shock, search must be made for some perpetuating factor or factors. It is certain that in the late stages of shock there is a *generalized* increase in capillary permeability. Bell, Clark, and Cuthbertson (1938) believed that a generalized fluid loss plays some role in traumatic shock. This generalized fluid loss may result from or be associated with one or more of the following factors. It is to be remembered in each case, however, that these may not be causative agents, but merely evidences of general cell injury. Even the increased capillary permeability may not be a causative but merely an associated change.

POSSIBLE PERPETUATING FACTORS IN SHOCK

1. Anoxia
2. Hyperpotassemia
3. Adrenal medullary overaction
4. Adrenal cortical insufficiency
5. Histamine or other tissue metabolites
6. Nervous factors

1. Anoxia.—The importance of anoxia in shock has been recognized for some time and Cannon in his book (1923) devotes considerable attention to it. That its importance continued to be recognized considerably more recently is evidenced by a quotation from the next book on shock (Moon's) appearing in 1938: "Anoxia probably is the most important factor tending to increase or perpetuate the circulatory deficiency." Krogh, as early as 1922, recognized the vicious circle in shock and the possible role of anoxia in it, stating:

"A very essential feature in the aetiology of shock is the vicious circle, which is set up by the poisoning of the capillaries. When the circulation begins to fail the blood supply to the tissues suffers and this in turn leads, by reason of oxygen lack or by reason of the diminished supply of tonic hormone, to still further dilatation. At more advanced stages the permeability of the capillary wall is so far increased that loss of plasma occurs, thus aggravating once more the failure of the circulation."

One could go even further back to find references to anoxia. Moon (1938) states that John Hunter advised oxygen in the treatment of shock. Professor Leonard Hill of London (1910), who believed shock was caused by "a paralysis of the synapses by a widespread injury which caused a defective transmission at these points," was an early advocate of the administration of oxygen to shock cases. The object was to "maintain the circulation which would allow the synapses to

recover." Bayliss (1918) realized the importance of anoxia in shock, stating: "At the risk of tiresome iteration, I would again emphasize the importance of adequate oxygen supply to the tissues."

Landis (1928) studied the effects upon capillary permeability of oxygen lack, of high tensions of carbon dioxide, and of increased hydrogen-ion concentration as observed in single capillaries of the frog mesentery. Direct measurements of fluid movement in cubic micra per square micron of capillary wall per second was correlated with the capillary pressure. After a three-minute period of oxygen lack, fluid filtered through the capillary wall at approximately four times the control rate. The increased permeability of the wall permitted also the passage of protein and thus reduced the effective osmotic pressure of the plasma proteins to almost one-half their normal value.

This fluid movement through the asphyxiated capillary wall was directly proportional to the difference between capillary pressure and the effective osmotic pressure of the plasma proteins, indicating that the wall, although more permeable than normal, still acted as a passive filter. When normal circulation was restored, the capillary wall soon recovered its impermeability to protein and the rate of fluid transudation was also reduced almost to normal.

The effect of carbon dioxide was only slight, even complete saturation of the perfusing fluid increasing transudation only slightly, and the wall remained normally impermeable to protein. Increase in hydrogen ion concentration within normal limits had little or no effect, though at pH 4 the characteristic effects of injury appeared.

The whole question of anoxia has been further developed by the important work of McClure, Hartman, and their associates (1935-1939). These authors first investigated the effects of artificial fever therapy. The pathologic changes resulting from this treatment in both human cases and experimental animals were engorgement of the blood vessels, especially the capillaries, and hemorrhage and cellular degeneration. The most marked changes occurred in the brain, lungs, and adrenals, with hemorrhagic encephalitis, hemorrhagic pneumonia, and hemorrhagic degeneration of the cortex respectively. Death occurred from vascular collapse. Chemical analysis revealed that these changes were closely related to the development of anoxia. The combination of depressing action of sedatives, such as sodium amytal, usually given to fever therapy cases, with the increased demands for oxygen due to the increased metabolism associated with the hyperpyrexia, exaggerated any other factors decreasing the oxygen supply.

The pathologic changes were similar to those of anoxia produced in other ways. They could be prevented by the administration of oxygen throughout the fever treatment, provided respiration and blood pressure were maintained at reasonable levels.

The work of Courville (1936) on the anoxic changes in the brain following nitrous oxide anesthesia led to renewed interest in the importance of anesthesia in shock. The following quotation from Courville's article is of interest:

"As a rule these patients developed respiratory or cardiorespiratory failure while under nitrous oxide-oxygen anesthesia and failed to regain consciousness when the anesthetic was withdrawn. During the survival period the patients remained in coma, frequently had convulsions and most of them died in a state of hyperthermia after an interval of 1½ to 26 days. A few individuals recovered, some with a residual lenticular syndrome, others with a permanent psychosis, while some fortunately recovered completely. In the fatal cases the cerebral cortex and the lenticular nuclei presented areas of necrosis which at times became confluent and if the survival period was sufficiently long, resulted in astrovascular scars."

McClure, Hartman and their associates (1939) extended these studies to cover the effects of most of the present-day anesthetics and the various premedications used with them. These authors also did numerous blood oxygen tests on human beings under anesthesia and on experimental animals. They found that evipal and other barbiturates in full doses were especially culpable, and that in large doses morphine was as well. This latter point is of especial interest to the whole shock problem, since morphine is so widely used as a means of shock treatment. This use, largely empirical, is chiefly a result of the imputations of the older nervous therapy of shock. Possibly quantitative experimental studies may prove this empiricism in error.

Davis (1937) decided to make metabolic determinations by means of a Krogh respiratory apparatus to follow the rate of oxygen consumption in secondary shock. In normal dogs it was found that the intravenous injection of normal salt solution increased the rate of oxygen consumption by 25 to 50 per cent. The maximal increase followed the introduction of 1,400 to 2,400 c.c., and with more solution a plateau in the curve is maintained. The tolerance for water was found to be great in normal animals, and up to 25 per cent body weight of normal saline solution could be given without deleterious effects. Davis found that in traumatic and hemorrhagic shock, on the other hand, a peculiar alteration of the metabolic response to fluids occurs. The maximal increase in the rate of oxygen usage is reached at an earlier stage of the fluid injection; i.e., after 700 to 1,200 c.c. of the fluid have been given. Further administration results in a progressive decline in the rate of oxygen consumption, only 5 to 12 per cent body weight of fluid producing a fall in the metabolic rate. Along with these metabolic changes in secondary shock, there is a marked alteration in renal function, the water diuresis being minimal even after large infusions.

Davis called this diminution of oxygen usage after fluid administration in secondary shock the "anoxemic response" and believed it may be due to one of three factors: (1) insufficiency of oxygen available in lungs; (2) decrease of oxygen-carrying capacity of the blood stream; and (3) interference with oxygen utilization by the tissues.

He ruled out the third factor by showing that in normal animals excess fluid administration even to the point of edema caused no decrease in oxygen consumption. Furthermore, the pulmonary edema did not seem to be the cause of the anoxemia, although Davis did not give detailed data in this regard. He concluded in favor of the second factor, saying: "It is suggested, therefore, that the augmentation of the anoxemia of shock by fluids is the result of loss of protein and cells into the traumatized area, the peritoneal cavity and to a lesser extent into the alveoli of the lungs and general tissue spaces." It is difficult to follow the reasoning here as the plasma protein, which is washed out, is of relatively slight importance as a carrier of oxygen in comparison with the hemoglobin.

Other workers have emphasized anoxia. Thus, Andrews (1935) pointed out the danger of anoxemia during surgical operations and attributed some cases of shock to it. Meek (1936) also realized the importance of anoxia in shock, stating that shock is followed by a set of pathologic-physiologic reactions and "the most important of these are the production of tissue anoxemia and increased capillary permeability."

It might be mentioned parenthetically at this point that use of the term "anoxia," as adopted by Hartman, is preferable to "anoxemia" except in cases where one is referring specifically to blood.

Anoxia in shock was studied by Mertens (1938) and Schwarz and Malikiosis (1938) in Germany. The observations of Kabat and Dennis (1938, 1939) and Dennis and Kabat (1939) on cerebral anemia indicate the importance of anoxia, but the animals did not develop a shock-like condition. This indicates that anoxia of the brain alone may not be a prime factor in producing irreversible shock. The importance of anoxia might be further exemplified by a quotation from Moon (1938): "So far as the actual mechanism is concerned, many phenomena called toxic are essentially anoxic." Crile's findings of degenerative changes in the central nervous system accompanying shock are explained on an anoxic basis by Moon (1938): "It is probable that the changes described are due to anoxemia and are the result rather than, as Crile supposed, the cause of shock." (Possibly this confusion of cause and result might be turned about towards some of the theories of Moon himself.) Sheehan (1940) reported a series of fatal cases of shock with subendocardial hemorrhages as a frequent finding. He stated that he believed they appeared too old to be due to terminal anoxia.

Freeman, Shaw, and Snyder (1936) found that not only was the blood flow through the hand in clinical cases of shock markedly reduced, but also that the low oxygen saturation of the venous blood indicated the severity of the tissue asphyxia. Tomb (1937), on the basis of Freeman's previous work, advised ergotoxine to relax the sympathetic nervous system plus oxygen inhalations in the treatment of shock. He stated: "All the symptoms of shock are directly referable [*sic*] to over stimulation of the sympathetic nervous system, and to consequent asphyxiation of the cells of the body through want of oxygen."

In experiments on dogs Wood, Mason, and Blalock (1940) studied the effects of inhalation of a high concentration of oxygen in shock. Shock was produced in three ways (hemorrhage, histamine, and trauma) and blood oxygen utilization studies were made by studying the oxygen content of the femoral, renal, and portal veins and of the venous blood from the whole body in the right heart. The inhalation of oxygen under these conditions resulted in a considerable increase in the amount of oxygen available to the tissues, as evidenced by a rise in arterial oxygen content and increases in the venous oxygen content of blood from the various sources listed above. This availability was possibly further enhanced by concomitant increases in carbon dioxide tension in consequence of the so-called Bohr effect (raised carbon dioxide tension increases the percentage of oxyhemoglobin dissociated at a given oxygen tension). Wood, Mason, and Blalock concluded that their results indicated that inhalations of high concentrations of oxygen exert a beneficial effect in the treatment of peripheral circulatory failure.

Another direction in which oxygen therapy has been advanced is the use of high concentrations (80 to 90 per cent) of oxygen, as with the B.L.B. mask. This relieves the tissue anoxia present in so many cases. It is to be remembered that in many cases of shock accessory injuries impede oxygen intake as well as oxygen transport in the blood. Davis (1940), in a study of fifty necropsies following shock, emphasized the importance of anoxemia of the central nervous system. Varangot (1940) stated: "*Le blessé choqué meurt d'anoxémie.*"

Tannenberg (1939) has recently studied the pathologic effects of anoxic and insulin shock in rabbits. He found the effects of the two quite similar with definite cerebral changes somewhat reminiscent of Crile's "exhaustion" effects and changes in the cardiac muscle and liver. In the latter organ hydropic changes of hepatic cells were observed with occasionally definite focal necroses. The similarity of these changes to those occurring in burns is to be noted. Keeley, Gibson, and Pijoan (1939) found that in experimental burn shock the oxygen saturation of venous blood was reduced in all animals. The

values dropped to less than 10 per cent prior to peripheral collapse in those animals that succumbed. Ziegler and associates (1940) have recently reported that partial anoxia in dogs, produced by breathing an atmosphere containing 5 per cent oxygen, leads to a fairly marked decrease in plasma potassium.

Decreased Oxygen Consumption.—Some of the early work of Aub (1920) and others on the decreased metabolism in shock indicated a decreased oxygen consumption. Gesell, Blair, and Trotter (1922) found the oxygen consumption in dogs immediately following hemorrhage to be 29 per cent below the control figure. Bearing on the question of anoxia are the experiments of Schlomovitz, Ronzone, and Schlomovitz (1924), who studied experimentally the oxygen consumption during repeated slight bleeding. At first there was little change, but after about 1.5 to 2.5 per cent body weight was removed by bleeding, a marked decrease in oxygen consumption occurred. Related to the decrease in oxygen consumption and decreased metabolism, there is a fall in body temperature accompanying shock. Kinnaman (1903) stated in this regard: "As shock increases in severity, the most uniform and progressive factor is the fall in temperature." Other studies on the oxygen consumption include those of Schneider (1938) and Bansi (1938) in Germany and Davis (1936, 1937) in this country. Davis found a decreased metabolism and concluded (1936) that "shock is accompanied by a marked fall in the rate of oxygen consumption." It will be mentioned again in conclusion that the classification of anoxia as a perpetuating factor in shock is somewhat arbitrary. It certainly is to some extent an accompanying factor as well.

2. Hyperpotassemia.—The importance of hyperpotassemia has been re-emphasized by the recent studies of Scudder and his associates. Potassium is of importance not only in the body of the victim of shock, but also in the blood that he may receive during treatment. It thus has a dual importance and deserves attention at this time. That potassium changes are not an important initiating factor in shock is indicated by the lateness of their onset. They seem to be associated with general cell damage and may thus be either merely an accompanying or actually a perpetuating factor in shock.

The observations of Scudder, Smith, and Drew (1939) on the plasma potassium content of cardiac blood at death are of interest. These authors found that in pathologic states, caused by intestinal obstruction, intestinal fistula, hemorrhage or trauma, the concentration of potassium in the cardiac blood at death in the cat averaged 42.8 mg. per cent. In four dogs poisoned with potassium this average was a little higher, 59.5 mg. per cent. The average venous plasma potassium in sixty young human adults was 17.2 mg. per cent (range 13.5 to 21.5). The average plasma potassium of human cardiac blood taken

at death was 29.8 mg. per cent. These authors concluded, therefore, that the human cardiac muscle is more susceptible to potassium than that of certain other animals. This conclusion is true, of course, only if the hyperpotassemia was the cause of death, but the authors do not state that.

More recently, Scudder, Corcoran, and Drew (1940) have extended the observations on the increase in serum potassium to cadaver blood. In twenty-seven cases the average concentration of the serum potassium was 101 mg. per cent. This high value is approximately 3.5 times the concentration found at death and nearly 6 times normal values. Experiments indicated that ammonia production might be responsible for this rapid diffusion of potassium from the cells into the serum. Furthermore, it was believed that the diffusion was accelerated by the fact that the cadavers were not placed immediately in a refrigerator. The writer spent two days in Youdine's laboratory and learned the type of case that Youdine used for obtaining cadaver blood. Only one of Scudder and his co-workers' twenty-seven cases would strictly come under this head; namely, a case of multiple fractures of the skull with a serum potassium of 72. Since this reading is elevated, although not as markedly as the average of the others, Scudder's point is not much weakened. Drew, Edsall, and Scudder (1939) have recently reported that, while there is little loss of red cells over a period of thirty days in heparinized blood, the plasma potassium content increases tenfold.

De Gowin, Harris, and Plass (1940) found that during blood storage, the potassium of the erythrocytes diffused into the plasma where it attained a maximum concentration in two weeks. Transfusion into human beings of blood with maximum plasma potassium was accompanied by no clinical, chemical, or electrocardiographic evidence of toxicity. It is to be remembered, however, before applying this dictum too literally that there is enough potassium in 3 liters of blood to cause death. Therefore, avoid transfusion of preserved blood in large amounts.

Zwemer and Scudder (1937) produced shock in cats by extensive crushing of tissue, intestinal manipulation, acute pancreatitis, intestinal obstruction, and hemorrhage. These animals developed blood potassium levels similar to those found in animals with severe adrenal insufficiency or shocked by intraperitoneal injections of potassium salts. Rises of 50 to 100 per cent were not uncommon and high potassium levels were also found in the fluids obtained from closed body cavities. These authors concluded on the basis of the findings:

"Since the effect of excess potassium in extracellular body fluids is in many respects similar to that of histamine, and as injections of histamine are followed by increased blood potassium (Thaler), our

findings are not inconsistent with those of Cannon, who holds that shock is due to a histamine-like substance."

In direct opposition to Scudder and associates (1937) with regard to the rise of plasma potassium following high intestinal obstruction is the paper of Greenwood, Haist, and Taylor (1940), of Toronto. These authors found that the plasma potassium fell in all of their animals from 17 to 40 per cent of the initial values during the first few days after operation. A post-mortem rise occurred in some cases, but was considered to be of little probable importance. These authors concluded that "in dogs changes in plasma potassium do not play an important part in causing death following acute intestinal obstruction."

Brewer, Larson, and Schroeder (1939) have also studied plasma potassium. These authors found that a single injection of 1 c.c. of 1:1,000 adrenalin would give a transient rise in potassium content from

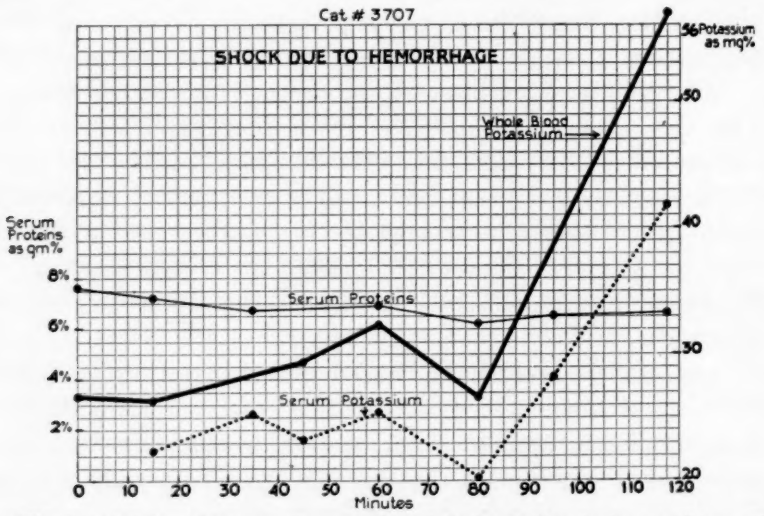


Fig. 3.—Blood potassium increase in experimental shock due to hemorrhage. (From Zwemer, R. L., and Scudder, J.: SURGERY 4: 515, 1938.)

a normal of 17 to 18 mg. per cent to a level of 19 to 22 mg. per cent. The rise was more marked in arterial than venous blood and was followed by a fall to below the previous normal level. This effect was observed in both dogs and man. Swingle and colleagues (1938) found no significant change in the serum potassium accompanying fatal adrenalin shock in normal or adrenalectomized dogs. They even said: "It is obvious that adrenalin shock has no relation to serum electrolyte changes. . . . In none of the experiments on either intact or adrenalectomized dogs were we able to correlate the shock symptoms and circulatory collapse (from adrenalin injections) with either hemoconcentration or serum electrolyte changes."

Zwemer and Scudder (1938) found the blood potassium to be increased in experimental shock. On the other hand, Bisgard, McIntyre, and Osherhoff (1938) found that in traumatic shock there was "no

consistent alteration of sodium, potassium, or chlorides." These latter authors also found no consistent change in high intestinal obstruction. This is consistent with the results of Jorgensen, Dietz, and Hill (1940), who concluded that "hyperpotassemia cannot be considered as a contributing factor to the cause of collapse and death in experimental intestinal obstruction in the dog."

The review of Scudder, Drew, Corcoran, and Bull (1939) of their studies on blood preservation includes observations later presented in Scudder's book. Important conclusions include:

1. Potassium transfer from cells to plasma begins as soon as blood is withdrawn. At the end of ten days 25 per cent may have left the cells, and at the end of thirty days 50 per cent. The rate is influenced by the following factors: (a) Shaking increases the transfer. (b) The size of the plasma cell interface in a bottle where the cells have settled is of great importance. The authors suggested tubes rather than wide flasks, and later (1940) advised hourglass-shaped bottles.

2. Potassium diffusion occurs independently of hemolysis.

The observations summarized in Scudder's book (1940) are of especial importance in considering the importance of hyperpotassemia in shock. Scudder observed twenty-eight cases of shock, twenty-six of which showed changes in the plasma potassium. A 100 per cent mortality occurred in those having an increase of over 100 per cent in the plasma potassium value. In contrast there were no deaths in the group showing an increase up to 25 per cent. A 71 per cent survival rate occurred in the cases with increases up to 50 per cent; whereas, in those whose plasma potassium had increased between 50 and 100 per cent, only 38 per cent lived. Concurrent sepsis tended to make the values low, even when the condition was serious.

Experimentally, Scudder found in 28 cats that hemoconcentration and hyperpotassemia often occurred. That the former preceded the latter casts some doubt on the probability that the latter is an *initiating* factor in shock. Further discussion of Scudder's work is included in the section of the present review devoted to his book.

Many previous workers studied potassium changes. Sunderman (1931) studied a series of pneumonia patients and found that the potassium concentration in the serum was increased in over one-half the patients. Atchley, Richards, and Benedict (1931) studied blood electrolyte changes during histamine shock in dogs. An increase in total serum base invariably occurred, but, in the only case where the potassium was determined separately, it showed no significant change. An excellent review of the potassium changes in shock was made by Eppinger (1938), of Vienna.

In the dogs in the series of Swingle and his co-workers (1938) the serum potassium did not increase in the animals subjected to intestinal

stripping, and the general tendency was for this electrolyte to decrease when the animal was in collapse. Only two of the six dogs subjected to muscle trauma showed a significant potassium increase. This increase seemed to be more dependent on the time interval since the trauma than on the severity of the circulating failure and shock. It should be remembered that these experiments involved the use of adrenalectomized rather than normal dogs. Recently Fenn, Wilde, Boak, and Koenemann (1939), of the University of Rochester, have shown that partial or intermittent occlusion of the arterial blood supply of a muscle results in an increase in the potassium content of the venous plasma. Excessive slowing or complete stagnation did not seem to increase further the amount of potassium. Stewart and Rourke (1938) reported a lowering of serum potassium associated with operation and ether anesthesia in human beings. In none of these patients, however, was the blood loss more than 13 per cent of the blood volume. Myers and Muntwyler (1940) have recently reviewed the significance of potassium changes in the blood. Scudder (1940) advised gastric lavage to wash out the high potassium containing gastric secretion present in shock. Lucena, Peregrino, Ramos, and Bethlem (1940) noted an increase in blood potassium and decrease in the sodium following surgical operation. Larson (1940) has demonstrated that epinephrine injections depress the serum potassium level in cats. This would make the potassium elevation theory of shock hard to fit in with the syndrome of epinephrine shock. Stickney (1940) found no relation between the potassium balance in resting muscle and adrenalin injections. Zwemer and Truszkowski (1936) discussed the relationship between the adrenals and potassium.

3. Role of the Adrenal Medulla. Vasoconstriction in Shock.—The historical development of the concept that the vasomotor center is intact and the peripheral vessels constricted in all but terminal shock has already been traced. The role of overaction of the adrenal medulla, as a factor not only in producing this condition, but actually in partly causing the shock itself, has recently been re-emphasized, especially by Freeman (1933, 1935). Freeman and also Tomb (1937) have even suggested the possibility of ergotoxine in the treatment of shock to counteract this overaction of the sympathetics. Early views on this subject of adrenalin include those of Henderson, Prince, and Haggard (1917): "We conclude that prolonged excessive secretion of epinephrin (if it occurs under pain) is not a critically important factor in the production of shock. It is therefore improbable that surgical shock is a result of excessive secretion of the suprarenals secondary to sensory stimulation."

Freeman's hypothesis is that the vasoconstriction associated with shock is not only an accompanying but also a causative factor. Freeman, Shaffer, Schecter, and Holling (1938) stated: "Vasoconstriction

after hemorrhage serves to protect the vital centers against the harmful effects of a dangerously low blood pressure.'' This action protects the vital centers but causes decreased blood flow in the remainder of the body. This gives stasis and increased capillary permeability, and the resultant loss of fluid renders the shock worse. Thus, an essentially protective mechanism results in a vicious circle. The peripheral tissues are not so important qualitatively, but quantitatively their action in fluid loss is of importance. In the sympathectomized dog this preferential treatment was found to be lost, and minor hemorrhages did not result in such a marked blood pressure fall. The sympathectomized dogs were not able, however, to tolerate as extensive hemorrhages as the normal dogs. In all these experiments the peripheral blood flow seemed to be a more accurate prognostic index than the blood pressure. Freeman (1933, 1939) also showed that prolonged activity of the sympathetic nervous system, whether resulting from the injection of adrenalin or from the spontaneous activity of the pseudaffective state, resulted in a decrease in the circulating blood volume. This decrease could be prevented by complete sympathectomy.

That the adrenal medulla is overactive in shock is substantiated by the presence of an elevated blood sugar, as shown to be the case in postoperative shock by Gale (1935) and others. Bedford (1917) recognized the increased activity of the adrenals in shock, stating: ''Increased quantities of epinephrine are thrown into the blood during conditions of low blood pressure and shock.'' The studies of Doménech-Alsina (1933), indicating the decreased sensibility to adrenalin in certain shock states, fit in well with the idea that the animal organism itself has an increased production of adrenalin during shock. Doménech-Alsina (1937) in experiments on dogs concluded that the maintenance of arterial pressure after hemorrhage does not have a direct relation to the production of adrenalin. This is somewhat in opposition to the results of several workers, including Bedford (1917) and Tournade and Chabrol (1925). Schlossberg and Sawyer (1933) found that sympathectomized cats were more sensitive to hemorrhage than normal cats.

Davis (1937) compared shock produced by repeated hemorrhage, trauma to the extremities, and injections of adrenalin or histamine. He found that in adrenalin shock the tissue changes do not resemble those produced by hemorrhage or trauma. The lungs are much more edematous and the heart is always dilated. The liver frequently shows areas of vacuolization of the hepatic cells with areas of central necrosis which are not found in shock resulting from trauma or hemorrhage. Other differences are that in adrenalin shock the thyroid gland shows a vacuolization and some disappearance of the colloid in the acini and a mild hypertrophy of the living epithelium. In histamine shock there

are evidences of extreme vascular congestion in the splanchnic and thoracic viscera. Davis concluded: "The tissue changes present in adrenalin shock differ from those of hemorrhage and trauma, and this does not lend support to the concept of an excessive adrenal activity playing the major role in secondary shock."

Hamlin and Gregersen (1939) obtained results at variance with those of Freeman (1933). These authors used unanesthetized cats and found that in both normal and sympathectomized animals adrenalin caused an increase in plasma volume. Normal cats anesthetized with nembutal do show a reduction in plasma volume, but this is so slight as not to cause the volume to fall below the preanesthetic level. It would be of interest at this point to compare dosages, for different workers used different amounts of adrenalin.

Freeman (1939) 0.008 mg. adrenalin per kilogram per minute for 90 min.

Hamlin and Gregersen (1939) 0.35 mg. adrenalin per kilogram per minute for 24 min.

Swingle et al. (1938) 0.010 to 0.015 mg. adrenalin per kilogram per minute for 60 min.

These doses are considerably larger than those used by Prohaska, Harms, and Dragstedt (1937) for their chronic hypertension experiments where no shock resulted (namely 0.0009 to 0.003 mg. per kilogram per minute). It would seem that several factors would have to be considered besides the dosage; first, the duration of the injection, and second, whether the injection kept the blood pressure elevated, indicating decreased peripheral blood flow.

Other work has been recently reported having a bearing on this aspect of the shock question. Penner and Bernheim (1939) recently surveyed the post-mortem records of the Mount Sinai Hospital, New York City, for the last ten years and found forty cases of acute post-operative and diphtheritic enterocolitis. These followed a number of conditions, but "the one finding that was present in all the cases was shock." They postulated that the shock gave decreased blood flow and vasoconstriction in the intestines with resultant anoxemia of the wall and finally transudation of plasma and even necrosis. The work of Rein and Rössler (1929) tends to support this view which explains the engorgement of intestinal villi, etc., occurring in shock as well as does Moon's toxemia theory. In one of Rein and Rössler's experiments a blood loss equaling 2 per cent body weight resulted in a 20 per cent drop in blood pressure in eight minutes. Simultaneously the flow through the intestine decreased 70 per cent and through the femoral artery 82 per cent. Ten minutes after cessation of the bleeding the blood pressure was only 5 per cent below its control value and the femoral artery flow had actually risen to 30 per cent above the initial

value, but the intestinal flow was still 20 per cent below its original state.

The recently developed "digital plethysmograph" by Johnson (1940), of St. Luke's Hospital, Chicago, may furnish new information on clinical shock problems. This instrument records graphically the pulse waves in a finger. While other types of peripheral and central circulatory conditions have been studied, so far it has not been applied to shock cases. This instrument does not record the absolute pressure, merely relative pressures and volume changes in the form of a pulse wave.

Observations upon *capillary pressure* have been made by Szántó (1937), of Budapest. This author observed the capillary pressure determined according to the method of Herzog in a series of operative cases. Readings were taken preoperatively and at varying intervals after operation. Minor operations caused little change, but operations where shock occurred were followed by a fall in capillary pressure. Before operation the capillary pressure averaged 40 to 50 mm. Hg. After severe operations there was a fall of 10 to 15 mm. Szántó concluded: "Decreased capillary pressure may be regarded as a component part of surgical shock." It is to be noted that these decreases were not markedly greater in relative amount than the fall in arterial blood pressure which somewhat limits their specific value as a prognostic or diagnostic sign in shock.

In summary it would seem that the presence of adrenal medullary overaction with (secondary) overaction of the sympathetic nervous system and peripheral vasoconstriction definitely is a factor in shock. It certainly begins early in the course of shock, but whether it is an initiating, accompanying, or perpetuating factor is difficult to determine. Furthermore, if it is merely a symptom, so to speak, whether its treatment is of benefit per se or whether it is a protective mechanism and should be left alone has not been completely decided. For some years the author has made the empirical observation that this overaction of the adrenals may occur most markedly in young persons. If such a young person is submitted to an operative procedure accompanied by considerable loss of blood, he will show a much more marked primary elevation of blood pressure than older persons. It would seem as though the adrenals were either very easily stimulated or the pliable vessels of young persons especially easily constricted.

4. ROLE OF THE ADRENAL CORTEX. HORMONE REGULATION OF CAPILLARY PERMEABILITY.—The function of the adrenal cortex is intimately tied up with that of the adrenal medulla and with the regulation of the sodium-potassium balance in the body. Early work on the significance of the adrenal cortex chiefly centered around the similarity between shock following adrenalectomy and other types of shock. Latterly, attention

was paid to the treatment, both therapeutic and prophylactic, of shock states with adrenal cortical hormone, both synthetic and natural.

Shock Following Adrenalectomy.—It has been known for some time that bilateral adrenalectomy will cause shock and death. Early studies of the Princeton group, including Swingle, Pfiffner, Parkins, Vars, Bott, Donahue, Taylor, and Hays (1933-1937), have shown that such shock is quite similar to surgical and traumatic shock and that, furthermore, adrenalectomized dogs are more susceptible to various agents commonly known to produce shock (intestinal stripping, hemorrhage, trauma, etc.). Those authors also showed that the various physiologic and chemical changes accompanying such shock due to adrenalectomy could be largely prevented or, if present, relieved by adequate adrenal cortical hormone dosage. In fact the similarity to shock was so striking that Swingle, Pfiffner, Vars, Bott, and Parkins

TABLE VII

CONDITIONS EXISTING IN ADRENAL INSUFFICIENCY (ANIMALS) AND TRAUMATIC SHOCK (MAN)

(From Swingle, Pfiffner, Vars, Bott, and Parkins (1933)

1. Blood volume	Decreased
2. Blood pressure	Decreased
3. Hemoglobin	Increased
4. Hematocrit	Increased
5. Red cell count	Increased
6. Venous pressure	Decreased
7. Rate blood flow	Decreased
8. Blood viscosity	Increased
9. Hemoconcentration	Increased
10. Cardiac output	Decreased
11. Venous return to right heart	Decreased
12. Heart rate	Increased
13. Heart condition	Normal apparently
14. Weak, fast pulse	Present
15. Vasoconstriction	Present
16. Ability to dilute	Lacking
17. Blood nonprotein nitrogen and urea	Increased
18. Alkali reserve	Decreased
19. Basal metabolism	Decreased
20. Blood sugar	Decreased in adrenal insufficiency Normal or slightly above in traumatic shock
21. Body temperature	Decreased
22. Use vasoconstrictor drugs	Ineffective
23. Effect forcing fluids	Beneficial
24. Vasomotor center	Normal apparently
25. Sensitivity to painful stimuli	Decreased
26. Sensitivity to cold	Increased
27. Sensitivity to anesthetics	Increased
28. Sensitivity to histamine	Increased in adrenal insufficiency, action unknown in shock
29. Sensitivity to infections and toxins	Increased
30. Urine volume	Decreased
31. Sensitivity to hemorrhage	Increased
32. Sensitivity to trauma and operations	Increased

(1933) presented a table (see Table VII) showing that of thirty-two different factors, all but two were similar to shock and hemorrhage, and one of these was not definite.

The one discrepancy, as they pointed out, is that in adrenal insufficiency the blood sugar is low, while in traumatic shock it is normal or elevated. Freeman (1933) took this as a point of departure to disagree with Swingle and associates and while agreeing with them that a type of shock certainly follows adrenalectomy, this does not mean that adrenal insufficiency is the cause of all shock any more than, since insulin shock resembles ordinary shock in many particulars (and it it to be noted also gives a low blood sugar), therefore, all shock is due to hyperinsulinism.

Swingle and co-workers (1938) performed other experiments on the reaction of adrenalectomized dogs. These dogs developed fatal shock when submitted to various traumatizing procedures (i.e., intraperitoneal glucose injection); whereas, animals primed with hormone reacted like dogs with normal adrenals. The adrenalectomized dogs exhibiting circulatory collapse promptly reacted to intravenous injections of hypertonic saline solution with restoration of blood pressure and hemoconcentration to normal. The effect was temporary and the fluid was not held in circulation unless cortical hormone was given. The writers attributed the cause of death from adrenal insufficiency to "capillary atony, with resulting dilatation, stasis, and peripheral vascular stagnation and believe that the cortical hormone is concerned with the maintenance of capillary tone and therefore regulatory control of the volume capacity of the circulatory system."

Swingle and co-workers (1937) extended their work to show that losses of water and electrolytes to the exterior of the body by way of the urine are not *necessary* accompaniments of adrenal insufficiency in dogs.

Swingle and co-workers (1938) have recently modified their earlier views (1935) to a contrary opinion in certain regards. They more recently held that in shock in adrenalectomized animals the hemoconcentration, when present, and loss of effective circulatory fluid volume are due to factors other than sodium or chloride and associated fluid changes. In their experiments the levels of serum sodium and chloride remained unchanged, even when the animal became moribund and it was evident that the circulatory collapse was not due to disturbance of the extracellular electrolyte pattern with resulting upset in the internal distribution of body water between extracellular (including vascular) and intracellular compartments.

In these experiments strong vigorous dogs who had been bilaterally adrenalectomized some months previously and kept on maintenance doses of adrenal cortical hormone were used. Seven were subjected

to intestinal stripping and six to muscle trauma. In most instances the amount of trauma was not such as to produce shock in normal animals. Hemoconcentration to a rather marked degree occurred in some instances but not in others. It was apparent, therefore, that in the type of animal employed in these experiments hemoconcentration is not a necessary accompaniment of shock. In those cases where it does occur, fluid was lost both locally and generally. These writers stated in this regard: "We do not attribute the increased permeability of the capillaries directly to lack of cortical hormone; rather, we assume, that it is due to the general capillary atony, dilatation and stasis which results from lack of hormone."

Adrenal cortical hormone exerted a very striking effect in reviving the animals in the experiments by Swingle and associates and in restoring the blood pressure. Hypertonic saline solution given intravenously when profound shock existed raised the arterial pressure to normal levels. In the absence of cortical hormone, however, the effect was temporary and the animals soon lapsed into a shock state. The significance of these experiments is yet to be finally determined.

Swingle and co-workers (1938) performed intestinal manipulation experiments on adrenalectomized dogs that led them to conclude that the cortical hormone exerts a direct effect upon blood pressure which is distinct and separable from the action of the hormone upon blood volume and fluid and electrolyte distribution. When the dogs were in collapse following the manipulative procedure, an intravenous injection of 3 c.c. per kilogram body weight of hormone was given, followed by gradual but steady improvement in the blood pressure. Since the serum electrolytes (Na, K, Cl) showed little change in these experiments, and, since about one-half of the dogs did not show hemoconcentration or loss of extracellular fluids when in profound shock, the hormonal action seemed to have a somewhat specific blood pressure raising function. Other observations include those of Britton and Silvette (1933), who reviewed the theories of corticoadrenal function. The especial importance of urinary chloride determinations in Addison's disease has been stressed by Butler, Power, and Wilder (1938). Weil and Browne (1939) reported an increased excretion of cortin in the urine after surgical operations.

Therapy of Shock With Cortical Hormone.—Early observations on the value of adrenal cortical extract include those of Marmorston-Gottesman and Perla (1931). These authors found that adequate cortin injections could bring the resistance to histamine of suprarenalectomized rats almost to normal. Reed (1938) studied the use of adrenal cortical extract in obstetric shock.

The results of Heuer and Andrus (1934) furnish additional evidence for the efficacy of adrenal cortical extract in at least certain types of

shock. These authors found that the intravenous injection of aqueous extracts of fatal high intestinal obstruction loops caused a primary and secondary fall in blood pressure. The latter was associated with a loss of plasmalike fluid from the circulating blood. Immediate injection of adrenal cortical extract had a marked effect both in prolonging the life of the animal and in preventing the drop in blood pressure and lessening the amount of plasma loss. Once shock had been present for an hour or more, however, neither intravenous saline solution, blood, etc., or adrenal cortical extract alone was of much avail. A combination of these treatments, on the other hand, had a markedly beneficial effect.

One of the most recent reviews of the use of adrenal cortical preparations in the treatment of Addison's disease is that of Ferrebee, Ragan, Atchley, and Loeb (1939). These authors used the synthetic compound desoxycorticosterone acetate or propionate (synthesized by Reichstein in 1935) and found very drastic effects. Over a ten-day period the following determinations showed a marked rise: serum sodium, body weight, serum volume, total blood volume, interstitial fluid volume, and systolic blood pressure. The following determinations showed a corresponding significant decrease: serum potassium, serum sugar, serum nonprotein nitrogen, serum protein, and serum cholesterol. Ragan, Ferrebee, and Fish (1939) studied the effect of desoxycorticosterone acetate upon plasma volume in patients during ether anesthesia and surgical operations. They found that the fall in plasma volume that occurred in control cases is not present when patients have been given desoxycorticosterone acetate subcutaneously three to four hours before operation. Perla (1939) reported that an excess of sodium chloride will markedly increase the resistance of rats to large amounts of histamine. Perla, Freiman, Sandberg, and Greenberg (1940) reported that desoxycorticosterone acetate and cortin combined with saline solution will prevent histamine shock in rats and mice and operative shock in human beings. The eleven patients upon whom the clinical conclusions were based might not have developed shock without the treatment, but at least did very well with it. A recent editorial (1940) in the *Journal of the American Medical Association* commenting on this article warned against too early enthusiasm.

Varangot (1940) favored the use of desoxycorticosterone in the prevention of shock. Selye and Dosne (1940) showed that desoxycorticosterone overdosage in the rat leads to hypochloremia and adrenal atrophy. Selye and Bassett (1940) have also recently shown that synthetic adrenal cortical extract (desoxycorticosterone) causes marked diuresis accompanied by increased chloride retention.

Selye and Dosne (1940) pointed out that, while pure corticosterone seems useful in the treatment of shock, even if all the slaughter house

material in North and South America could be secured, it would be insufficient to make such compounds available on a large scale. Thus, it took 400 pounds of cattle adrenal to make 50 mg. of pure corticosterone. Some hope is held out for obtaining sufficient quantities of corticosterone from the urine of domestic animals. The inefficacy of desoxycorticosterone seemed to indicate that the hydroxyl group on carbon atom 11 is important for the shock-combating action of adrenal steroids. Furthermore, the inefficacy of adrenal cortical extract mixtures is due to the presence of impurities which counterbalance the beneficial effects of the pure corticosterone.

Selye (1937) showed that the adrenal cortex hypertrophies following the exposure of an animal to a damaging agent. Weil and Browne (1939 and 1940) reported that cortin is excreted in the urine of patients under conditions of damage. In another article (1939) these authors stated that there is an increased excretion of cortin following surgical operations, reaching a maximum between the second and fifth postoperative days, and then gradually falling to the preoperative level. These experiments indicate an increased function of the adrenal cortex as a response to general organism injury.

Selye, Dosne, Bassett, and Whittaker (1940) studied experimentally the relation of the adrenals, thymus, and shock. They pointed out that mild trauma produces adrenal hypertrophy and thymus atrophy, the so-called "countershock phenomena." The countershock is caused, they believe, by increased adrenal cortical secretion. Preoperative administration of the latter would seem unwise, as it caused atrophy of the adrenals. These writers then went on to point out that desoxycorticosterone has proved inactive in their experiments on shock, while most cortical extracts were so crude as to be likewise inactive. They found that a reasonably pure cortin was effective in ameliorating shock in white rats produced by intestinal trauma or subcutaneous formaldehyde injection. Repeated small doses were necessary. They concluded as follows: "In the case of continued treatment with high doses of desoxycorticosterone the substance proved not only inactive but actually harmful."

At the same time as the article by Selye and co-workers (1940), Weil, Rose, and Browne (1940), also reporting from McGill University, offered further evidence for the value of adrenal cortical hormones in the treatment of experimental shock. Ether-anesthetized rabbits were given shock by means of trauma to the intestines. One group received cortin and desoxycorticosterone acetate, both preoperatively and postoperatively; the second group received preoperative desoxycorticosterone only, while the third control group received no medication. The first group had a mortality of 19 per cent and survived an average of 15 hours; the second group had a mortality of 46 per cent and survived an average of 14.6 hours, while the third

control group had a mortality of 62 per cent and survived an average of only 8 hours. These experiments indicated the relative inadequacy of desoxycorticosterone as compared with adrenal cortical extract, but this conclusion is rendered less definite by the introduction of a second variable into the experiments; namely, the absence of postoperative injections in some of them (*vide supra*).

Scudder (1940) also used cortical extract with salt solution clinically in twenty-seven cases. These included instances of postoperative shock, burns, hemorrhage, sepsis, intestinal obstruction, perforated duodenal ulcer, and acute pancreatitis. In general the results were good. A coincident hypopotassemia seemed to afford somewhat of a contraindication to the use of adrenal cortical extract.

The present status of the use of adrenal cortical hormone in the treatment of shock is hard to describe. The remedy seems to offer much promise, but the full extent of its usefulness and contraindications is not yet defined. Many of the clinical reports contain short lists of operations treated with cortical hormone without the development of shock that in my experience would not have developed shock even without cortical hormone if reasonable plasma balance had been maintained. There may be dangers in the use of cortical hormone, and Scudder (1940) has stated that in septic shock cortical extract may be harmful.

5. Toxins, Histamine, and Tissue Metabolites.—The toxic theory of shock was chiefly promulgated by Quénu (1918) in France and by the Shock Committee in England at the same time (Cannon and associates). Since this work was done shortly after the early work of Dale (1910) on histamine, this drug was the chief suspect. It is of interest in this connection to note that Sir Henry Dale recently stated: "With regard to the possible role of histamine, we know now, what we did not know then, that of all the major tissues of the body, the muscles contain least of that substance. Whatever else it may have been, the shock following the Bayliss-Cannon limb trauma was not histamine poisoning." The two questions now to be discussed are: (1) Is a toxin active in shock? (2) If so, is it histamine?

Histamine.—Of all the toxins imputed as being the cause of shock, histamine heads the list. There are probably two reasons for this fact: first, that histamine was one of the first autogenous vasodepressants to be studied considerably; and second, that the time of this study only shortly antedated World War I, when shock was also the center of attention. One of the earliest studies was that of Dale and Laidlaw (1910), who investigated the blood pressure depressing effects of histamine (β-iminazolylethylamine). This substance was found in depressor extracts of intestinal mucosa by Barger and Dale (1911). Further studies soon followed and in 1919 Dale and Laidlaw reported studies showing that, along with the fall in blood pressure

accompanying experimental histamine shock, there was a hemoconcentration, in some cases quite considerable (hemoglobin rise to 148 from a control of 96, and hematocrit rise to 50 from a control of 33). These authors attributed the hemoconcentration to an increased permeability of the peripheral vessels with outflowing of blood plasma. Atchley, Richards, and Benedict (1931) confirmed these findings in experimental histamine shock.

Shortly after Loewi and Dale focused attention on acetylcholine and other autogenous depressor extracts, in the early 1930's a new wave of interest involved the role of these substances in shock. Chang and Gaddum (1933) studied the mechanism of extraction of the substances affording new impetus by the advantages of their new chemical technique with trichloracetic acid extracts. Acetylcholine in particular was studied by Dudley (1933) and the work of Euler and Gaddum and others of Dale's associates at the National Institute for Medical Research (Hampstead) gave new information on acetylcholine, adenosine, H-substance, and other vasodepressants. The contributions of workers at the Institute are of great importance in the understanding of vasodepressor substances. This work, for which Dale received the Nobel Prize, includes the observations of Euler and Gaddum (1931) on the P substance, Dale and Gaddum (1930), Dale and Dudley (1931), Dale and Feldberg (1934), Feldberg and Gaddum (1934), and the comprehensive review of Dale (1934). The results of this work showed that histamine is only one of the many depressor substances.

There are still many advocates of the toxic theory of shock. Hooker (1920) was one of its supporters. Its popularity at the close of World War I is indicated by the following quotation from Krogh's monograph (1922) in which he referred to the Special Investigation Committee on Surgical Shock (1919): "The work of the Committee has proved conclusively that traumatic shock is due primarily to the action of toxic substances formed in the injured tissue."

König (1934), in Germany, believed that intermediary products of nuclear disintegration cause shock and collapse. Lurje (1936), in Moscow, advocated the toxic theory, finding a great increase in the amino acid nitrogen following operation. Aird and Henderson (1937) further showed that the histamine content of the peritoneal transudate from strangulated cat intestine increases until, after twenty-four hours of strangulation, it reaches a maximum of 1:5,000 to 1:20,000. The total content may amount to 4 mg., but they do not believe this is the sole lethal factor present.

The recent work of Minard (1937) has advanced the study of blood histamine. This author showed that in certain species, e.g., the rabbit, a large proportion of the blood histamine is in the platelet fraction.

In further experiments he used Barsoum and Gaddum's (1935) extraction method, which eliminates substances other than those of histamine-like character acting on the isolated guinea pig intestine. Minard's investigations revealed that blood returning from a traumatized extremity of a dog contains a distinctly greater amount of histamine-like substances than venous blood from the opposite normal extremity, the increase averaging 80 per cent in six experiments. No appreciable change was observed in the histamine equivalent of arterial blood and venous blood from normal extremities before trauma and after the animal was in profound shock. Minard was unable to state as a result of these investigations whether this local increase after trauma was or was not significant. Macdonald and Woolfe (1938), of Manchester, compared the histamine equivalents of the blood from normal and traumatized limbs in a series of cats, usually shortly before the death of the animal. The increase in this series was markedly less than that found by Minard (1937) and not even constantly present. These authors concluded that the slight rise might be due to ischemia of the tissues, and that there is little justification for assuming that histamine is liberated in significant amounts from damaged tissues in acute traumatic shock. Code and Macdonald (1937) also reviewed the histamine-like activity of the blood.

One of the most important blows to the histamine theory of shock comes from the paper of Dragstedt and Mead (1937). These authors showed that, while experimental shock could not be duplicated by intravenous histamine injections, subcutaneous and intramuscular injections would reproduce it in many respects. Testing the blood and thoracic duct lymph of these dogs for histamine gave positive results while similar dogs suffering from traumatic (trauma to intestines or extremities) shock gave negative analyses. They conclude:

1. "We failed to find any vasodepressor 'toxin' in the blood and lymph of dogs during experimental surgical shock."

2. "Experiments indicate that if the vasodepression of surgical shock was due to a toxemia such as that of histamine, the methods employed would have been adequate to detect it."

Phemister and Handy (1927) found no evidence of histamine in traumatized blood. Simonart (1928), Blalock (1930), and Herbst (1934) also found no toxin. Schneider (1930) found no evidence of toxins when he injected blood from traumatized patients into animals. Carlton (1935) opposed the toxemia theory and O'Shaughnessy and Slome (1935) stated: "Our first conclusion is that a toxemia due to the elaboration of histamine, or any other depressor substance manufactured in the traumatized area, plays no part in the syndrome of traumatic shock."

It is to be remembered that Moon advocated a toxic theory and showed pictures of tissues from histamine and traumatic shock both engorged while hemorrhagic shock gave dry organs. O'Shaughnessy and Slome (1935) reported findings quite contradictory to those of Moon. They stated: "The postmortem appearances in animals whose death has followed the administration of histamine differs [*sic*] significantly from those seen after death from traumatic shock." They then described the typical picture of histamine shock with its capillary congestion, congested viscera, etc., and continued: "In striking contrast to this, the characteristic feature after death from traumatic shock is a general pallor of the viscera, especially of the intestines, and of the omentum." Other data on Moon's theory are discussed in the section on his book.

However, histamine shock is not entirely dissimilar to traumatic or hemorrhagic shock, as shown by the experiments of Butler, Beard, and Blalock (1931). These authors determined the blood volume, plasma volume, red blood cell count, hemoglobin, and chloride content of blood before and after a low blood pressure had been produced by the subcutaneous injection of histamine, by the removal of blood plasma, and by the removal of whole blood. The injection of histamine produced alterations that were similar to those which accompanied the removal of blood plasma. Furthermore, histamine led to a decrease in the water content of striated muscle similar to that produced by trauma, by burns, and by the removal of blood plasma.

The experiments of Wilson and Roome (1936) are of importance with regard to the toxic theory of shock. These authors found that centrifugated extracts of traumatized limbs obtained by means of a hydraulic press caused no blood pressure fall when perfused in a second heparinized animal; indeed, a slight pressor effect was obtained. Similar extracts of traumatized muscle alone were slightly toxic but did not produce a sustained fall in blood pressure or death. Roome and Wilson concluded that: "The findings do not support the 'toxic theory' of the etiology of traumatic shock." Fender and Guptill (1936) interpreted their experiments as arguing against the presence of a toxic factor in traumatic shock. In two experiments a normal dog was connected to a traumatized dog for a period of two hours by blood vessel anastomosis and then separated. The normal dog recovered. These latter experiments are all right as far as they go, but they are too incomplete to prove anything.

Tissue Metabolites.—In this country general knowledge of the choline vasodepressor compounds has been especially advanced by Hunt and Renshaw (1930-1936) of Harvard University. Their studies are especially interesting in that they show that these substances are so often found occurring naturally in the body. It is of historical interest that Hunt and Taveau (1906) were the first to show the dramatic effect of

acetylcholine in lowering the blood pressure. Doménech-Alsina (1933) studied histamine hypotension. His researches indicated that loss of fluid at the level of the digestive tract is of probable predominant importance in the production of hemoconcentration in dogs following histamine administration.

The work of Lewis and his associates also tended to favor the importance of a histamine-like substance. The studies of Lewis and Harmer (1927) on the evidence for release of such a substance from injured skin, of Harris (1927) and other papers from the University College Medical School helped to advance this idea. More recently, the research of Barsoum, Gaddum, and Smirk (1935, 1936) at the University of Cairo has put forth new evidence for the histamine hypothesis. These authors have developed a new technique for determination of blood histamine, supposedly capable of detecting 0.02 γ per cubic centimeter of blood. They found more in the corpuscles than in plasma and found an increase after release of a constrictor to an extremity and after burns. The relation of the increase in burns to the presence of shock in that condition was so variable, however, that they stated: "The relation of this rise in blood histamine to secondary shock is uncertain. There was no clear evidence of any correlation between the blood histamine and the clinical condition of the patient." This is especially true since the blood histamine did not reach its maximum until an average of ten days after the burn, long after shock usually occurs.

The important work of Menkin (1936-1940) on inflammatory exudates has considerable bearing on the histamine hypothesis of shock. Exudates from burns and other types of human or experimental inflammatory processes were injected intracutaneously on a rabbit's abdomen. Simultaneous injection of trypan blue into the ear vein caused a marked collection of the dye around the abdominal wheal, indicating increased capillary permeability in that area. The active factor is nonprotein, nitrogenous, dialyzable, and precipitated by concentrated ammonium sulfate. It seemed, according to Menkin, to be an intermediary breakdown product of protein metabolism, probably belonging to the group of relatively simple polypeptides. It had no similarity to histamine. In a later paper (1939) he calls it "leukotoxine." This substance has both a permeability factor and a chemotactic factor. It does not contain histamine or resemble histamine as far as contractible effect on an isolated strip of guinea pig intestine. The studies of Cressman and Rigdon (1939) on capillary permeability and inflammation and the influences of narcosis on the degree of permeability are of interest in connection with Menkin's work. The recent work of Hughes (1939), of St. Mary's Hospital, London, on the capillary permeability-increasing factor of various inflammatory exudates is also of interest in this regard.

In line with the work of Menkin, Rigdon (1940) has shown that intradermal adrenalin inhibits the localization of trypan blue in areas of inflammation produced by xylol application. This xylol reaction (Rigdon, 1940) can be accentuated by a substance obtained from certain tissues of normal rabbits. The recent report of Lambert and Rosenthal (1940) on liberation of a histamine-like substance on stimulation of sympathetic nerves may lead to possible bridging of the gap between the "histamine" and "sympathetic overactivity" theories of shock. The further studies of Minard and Rosenthal (1940) on the use of thymoxyethyldiethylamine in counteracting certain histamine actions in dogs may be of therapeutic import.

Rose and Weil (1939) found that, during anaphylactic shock in the rabbit, a marked decrease in total blood histamine occurred, and that no increase in plasma histamine was observed. In a series of clinical cases with varying degrees of shock, as manifested by clinical signs, hemoconcentration and blood pressure fell and the blood histamine level was low, as compared with control values and those after recovery. The total blood histamine was also low in agonal states, and in shock cases the decrease was greater in the more severe instances. Rose and Browne in a second paper (1940) pointed out that this decrease may be due to localization of the histamine in the injured tissues or the gastrointestinal tract. Therefore, the absence of an increase in the blood does not necessarily mean that histamine is not an active factor in shock production.

The possible relationship between the histamine and the adrenal theories of shock might possibly be explained by the recent reports of Karady, Rose, and Browne (1940) working at the Royal Victoria Hospital, Montreal. Adrenalectomy produced a diminution in the histaminase content of the lungs of rats maintained on a standard diet and given normal saline solution to drink. If water were substituted for the normal saline solution, an even greater diminution occurred. Finally the diminution of histaminase in the lung tissue of the adrenalectomized rat could be restored to within normal limits by the administration of adequate amounts of cortin.

Feldberg and Kellaway (1938) and Feldberg, Holden, and Kellaway (1938) have made important studies on histamine liberation and action. They showed that "cobra venom contains a lecithinase which splits off oleic acid from lecithin. The resulting rest, lysocithin, is powerfully hemolytic." This substance can be tested for by injection into the anterior chamber of a rabbit's eye. The recent studies of Katz (1940), demonstrating that the sensitized rabbit cells will liberate histamine in vitro when placed in contact with antigen, have possibilities in the study not only of anaphylactic shock, but also of the histamine hypothesis of shock in general. Ramirez de Arellano, Lawton,

and Dragstedt (1940) have shown that trypsin will liberate histamine from tissues.

The possibility, therefore, is yet to be ruled out that tissue metabolites, not exactly toxins and not histamine, are active in shock. If so, they may be of importance in causing a generalized loss of fluid from the blood stream. On the other hand, even though present, they may be only secondary to some other process as anoxia.

6. Nervous Factors.—The nervous theory of origin of shock might be said to have been the leading theory up to the time of World War I, when Cannon, Quénu, and others introduced the traumatic toxemia theory. Both Meltzer's theory of inhibition and Crile's theory of exhaustion are variants of the nervous theory. At present it seems that the original nervous injury is seldom great enough to be an initiating factor in shock. Some, such as Mahaffey (1938) and Rehn (1937), still support the nervous theory. Rehn (1937) in his monograph entitled *Der Shock und verwandte Zustände des autonomen Systems* ascribes to just what he says in his title; that is, the nervous theory of origin. This work is largely based on "theoretical-clinical" reasoning.

Simonart (1928) concluded, as a result of experiments on cats, that an intact nerve supply is essential for the production of traumatic shock, but he has since modified this view. Blalock and Bradburn (1930) found the shock that results from central nervous system trauma to differ in important respects from the following hemorrhage. The role of the hypothalamus in the regulation of blood pressure has recently been reviewed by Leiter and Grinker (1934).

The paper of O'Shaughnessy and Slome (1935) introduced new evidence in favor of the nervous theory of shock and especially influenced London and Continental thought. One hundred cats anesthetized by chloralose (0.08 Gm. per kilogram body weight) were used in their experiments, which can be divided into the following groups.

A. *Experiments to Determine the Presence of a Possible Toxin.*—

1. *Occlusion of Venous Return:* O'Shaughnessy and Slome showed that ligation of the femoral vein (as practiced by Parsons and Phemister, 1930) or of the common iliac vein (as practiced by Holt and Macdonald, 1934) is insufficient to prevent completely the venous return from a limb. Effective occlusion was attained by ligature of the femoral vein and its tributaries in the groin and the external, internal, and common iliac veins, and the inferior vena cava and its transverse iliolumbar tributary. However, a limb, when so isolated, still produced lethal shock when traumatized.

2. *Perfusion of a Traumatized Limb:* This likewise gave no evidence of a toxin.

3. *Vividialysis:* This type of experiment also gave no evidence of a toxin.

O'Shaughnessy and Slome concluded from these experiments that toxins do not play a marked role in traumatic shock. They then continued with:

B. *Experiments to Determine the Extent of Fluid Loss by.—*

1. *Bisection Experiments:* In twelve cats the excess weight on the traumatized side averaged only 32 per cent of the calculated blood volume. Since some cats developed shock with only 20 per cent fluid loss, they argued that there must be some additional factor.

C. *Experiments to Test the Importance of the Nervous Factor.—*

1. Shock will occur even if the arteries to a traumatized limb are ligated. Previous workers had argued from the lack of shock after artery ligation that fluid loss is the dominant factor in shock. Because of lack of knee jerks in such a preparation, O'Shaughnessy and Slome refer to it as an "anemic limb" and postulate that the accompanying possible anesthesia may explain the lack of development of shock. If such a limb is perfused with the blood of a second cat, the first cat will develop shock after trauma. This shock is accompanied by a decreased bleeding volume and is apt to be fatal. This experiment is used to favor the nervous theory. Aside from its complexity, its chief objection is that the donor cat died before the traumatized animal.

2. *Nerve Blockage Experiments:* Blockage of nervous impulses by (1) nerve section, (2) spinal cord section, (3) spinal cord destruction, and (4) spinal anesthesia indicated that these procedures helped to prevent shock.

O'Shaughnessy and Slome concluded from these studies: "A toxemia due to elaboration of histamine or any other depressor substance manufactured in the traumatized area, plays no part in the syndrome of traumatic shock. We regard the two remaining factors, local fluid loss and the discharge of nociceptive nervous stimuli, as the effective etiological agents. The evidence does not allow us to dogmatize as to the relative importance of these factors, although we are inclined to believe that the nervous factor dominates the picture."

Three years later, Slome and O'Shaughnessy (1938) extended these experiments, and in addition, made records of nerve action potentials, showing them to be markedly exaggerated in the afferent nerves coming from a traumatized limb, even though the trauma had been produced some time before. These latter observations of Slome and O'Shaughnessy were not confirmed by Cressman and Benz (1939), who found no consistent increased barrage of nerve impulses in the nerves of the traumatized limb in an anesthetized animal. They occasionally found increased nerve impulses in nerves of untraumatized as well as traumatized extremities. Those present in shock may be due to impulses from the tactile and proprioceptive endings. In addition, these impulses might not be nociceptive.

The work of Shumacker, Lamont, and Metcalf (1939) on cross circulation of normal animals indicates the complexity of factors that may arise in shock cross-circulation experiments. Their studies show how poorly worked out are the control shifts of blood and fluid. Until the range of these factors is established, this type of experiment cannot be properly applied to the more complex question of shock. Or, in other words, if we don't know what happens when two normal dogs are cross circulated, how are we to appraise what happens when one of them is traumatized? Bell, Clark, and Cuthbertson (1938) did cross-circulation experiments, applying trauma to the transfused hindlimb of a recipient cat. A marked fall in blood pressure of the donor occurred, followed by death, while the recipient was practically unaffected. These results are the opposite of those of O'Shaughnessy and Slome (1935).

The experiments of Blalock and Cressman (1939) indicated that the type of anesthetic agent alone may have been an influencing factor in O'Shaughnessy and Slome's results. In the English experiments chloralose was used to anesthetize cats. Blalock and Cressman used both dogs and cats and both nembutal and chloralose in similar experiments. In none of the nembutal experiments was there evidence of the importance of nervous impulses in the genesis of shock. In cross-circulation experiments in which trauma was applied to a transfused hindlimb of the recipient animal no positive evidence as to the deleterious effects of nervous impulses was obtained, confirming the findings of Bell, Clark, and Cuthbertson (1938). The only positive evidence at all as to the importance of nerve impulses was obtained in the series of cats anesthetized by chloralose in which preliminary and repeated spinal anesthesia apparently exerted beneficial effects. This was not found in cats anesthetized by nembutal or in dogs anesthetized by either nembutal or chloralose. In these experiments local loss of fluid seemed to be the chief, even if not the only, factor.

The recent article of Lorber, Kabat, and Welte (1940) again swings the pendulum towards emphasis on the nervous factor in traumatic shock. These authors stated that their experiments were designed to test the reality of a nervous factor in traumatic shock and shed no light on the relative importance of this as compared with other causative factors. They found that shock could be produced in the perfused limb of the cat separated completely from the general circulation and communicating with the body only by means of its nerves. While this result agreed with that of O'Shaughnessy and Slome (1935), unlike these British authors, Lorber and associates found that deep anesthesia favored rather than hindered the development of shock.

The recent report of Freedman and Kabat (1940) tends to confirm that of Lorber, Kabat, and Welte (1940) that the nervous factor is

of considerable importance in traumatic shock. Traumatizing the hindlimbs of cats in a way to minimize fluid loss, shock still resulted. The average fluid loss in the traumatized limb was 0.85 per cent of the body weight. The means used to keep fluid loss at a minimum was to elevate the limb and keep it bandaged with three layers of adhesive tape. These authors found, in addition, that chloralose given following the trauma greatly increased the susceptibility of the animal to traumatic shock. Shock was effectively prevented in such experiments by preliminary transection of the upper lumbar spinal cord. Adrenalin produced a greater rise in blood pressure during shock than before trauma, except just before death when the response of blood pressure to adrenalin suddenly disappeared. Finally, as a result of this observation, these authors concluded: "No evidence was found to support the theory that hyperactivity of the sympathetic nervous system is responsible for the type of shock resulting primarily from afferent nerve impulses."

Volpitto, Woodbury, and Hamilton (1940) have shown that the arterial and venous pulse contours differ radically in cases of hemorrhage or traumatic shock as opposed to shock of neurogenic origin. Leveuf (1940) stated that in shock there is a relative overaction of the vagus and underaction of the sympathetic nervous system. This is, of course, contrary to practically all other published reports. The fact that Fender (1937) stimulated the splanchnic nerves of dogs for eight hours a day, six days a week, for five and one-half months without producing any lasting effect on the resting level of blood pressure might be an argument against the nervous theory of shock.

(To be continued in the March issue. The references will accompany the last part.)

Review of Recent Meetings

THE FIFTIETH ANNUAL MEETING OF THE WESTERN SURGICAL ASSOCIATION, DEC. 6 AND 7, 1940, TOPEKA, KAN.

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THE Western Surgical Association held its fiftieth anniversary meeting on Dec. 6 and 7, 1940. The scientific sessions were held at the Topeka Municipal Auditorium and the other events were held at the Hotel Jayhawk.

Herbert H. Davis, Omaha, Neb.: **Cystic Disease of the Breast. A Critical Review.**—The author opened his paper by reviewing different etiological theories. The endocrine factor is most popular. Davis believes that it is due to an abundance of the gonadotropic factor of the pituitary at the time when the ovarian factor is on the decrease, because most cases occur between 35 and 50 years of age, at which time the ovarian hormone decreases. He does not feel that the cystic type is important as far as a tendency to develop malignancy is concerned, but that the adenocystic type is important in this respect. His cases showed a greater occurrence of carcinoma than other reports in the literature. He found cystic disease distant from the carcinoma in numerous cases of carcinoma of the breast. Also, cases of cystic disease which later developed carcinoma were cited.

John Ogilvie, Kansas City, Mo., stated that he had relieved symptoms with estrogenic substance in large quantities, but, if the breast was removed later and examined, the pathologic changes were the same as if no estrin had been given. **O. J. Campbell,** Minneapolis, Minn., still feels that cystic disease is not a precursor to carcinoma except possibly in a few of the adenocystic cases. He said that two more of his previously reported series of 294 cases had developed carcinoma. Now a total of 5 have developed cancer.

Paul B. Magnuson, Chicago: **Joint Débridement; Surgical Treatment of Certain Types of Arthritis.**—The author stated that early stages of arthritis should be relegated to the medical service, while complications should be considered surgical. Marked changes in the joints are caused by wear and tear and overstrain. Toxemia, infection, and metabolic processes are only contributing factors. He showed some interesting experiments on dogs which demonstrated that cartilage never heals from side to side, but that, if an area is gouged out leaving normal edges surrounding the area, no disability results. Activity is necessary to produce a degenerative type of arthritis. He showed films demonstrating severe joint injury with no arthritis in contrast to mild joint injury which allowed the patient to use the joints and ultimately to develop arthritis. He showed cases with narrow joints with spurs and irregularities which he had operated upon with excellent results. He stated that all pathologic areas must be removed, allowing fibrocartilage to fill in and leave a good joint surface. He stressed the fact that it was not necessary to do a synovectomy. Early motion was recommended.

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Ralph G. Carothers, Cincinnati, Ohio: **Treatment of Cotton's Type of Fracture of the Ankle.**—Carothers mentioned the fact that, although Cotton's type of fracture is not common, it is not unusual. He said that it is one of the most treacherous types of fractures, but good results could be expected to follow good treatment. He gave a description of the fracture and methods of reduction. The mild group with no dislocation can be reduced with down and forward traction and marked dorsal flexion. The foot is held in this position and a good skin plaster cast is applied. The group in which there is a backward dislocation of the astragalus with a more marked deformity may be treated in a like manner, but there is a tendency for a recurrence of the dislocation. The group of severe fractures with both malleoli off presents a difficult problem and, if reduction cannot be obtained by manipulation, skeletal traction should be applied through the os calcis. In about ten days a skin plaster cast may be applied. Absolutely no motion should be permitted in the cast and no walking iron should be used. They are kept in plaster eight weeks, followed by an elastic bandage.

G. M. Morrison, Boston, pointed out that a few cases must be openly reduced. He described in minute detail the reduction with the warning that severe cases should have no weight-bearing for ten to twelve weeks. **Ralph M. Carter,** Green Bay, Wis., demonstrated his method of fixation which consisted of running Kirchsner wires through the bones of the foot, through the joint into the tibia to prevent slipping after application of the cast.

William R. Cubbins, Chicago: **The Conservative Treatment of Fractures of the Shaft of the Femur.**—A complete and detailed description was given of the conservative treatment used at Cook County Hospital, showing the simple Balkan frame and the low-hanging, large ring Thomas splint. Adhesive plaster traction can be used successfully but should not extend above the site of fracture. In order to prevent dermatitis due to adhesive plaster, the limb is not shaved. Cubbins showed films demonstrating the necessity of open reduction in some cases, as well as films of cases showing the misuse of plates, screws, etc.

Ralph M. Carter, Green Bay, Wis., stated that he preferred skeletal traction. **Francis E. Clough,** San Bernardino, Calif., stated that slow union should not be classed as nonunion, that heel pain meant pressure on the tendon achilles and not on the os calcis, and that cutting out the plaster over the heel aggravates the pain. The majority of cases are nonoperative. **Ralph G. Carothers,** Cincinnati, Ohio, stated that the maximum amount of weight should be used in the beginning. He said that metal plates applied in transverse fractures become loose because there is absorption of bone at the ends which produces a space between the bone ends and allows motion which loosens the screws.

Thomas G. Orr, Kansas City, Mo.: **Resection of the Head of the Pancreas and Duodenum for Carcinoma.**—The literature was reviewed, beginning with the 2 cases reported by Whipple in 1935 and including 14 cases subsequently reported. In Orr's case a cholecystectomy had previously been performed so that at the first stage the common duct instead of the gall bladder was anastomosed to the stomach and a gastroenterostomy was performed. Three weeks later a V-shaped excision of the pancreas, including the pylorus and duodenum, was performed. The patient was readmitted six weeks later, at which time a pseudocyst of the pancreas was drained and a pancreatic fistula resulted. This fistula was still persistent at the time of the report. There has been a 33.33 per cent mortality of the cases reported. Orr suggested that the use of lipocaic to prevent fatty infiltration of the liver might reduce this mortality.

Verne C. Hunt, Los Angeles, mentioned the large volume of pancreatic juice that drained from a pancreatic fistula in one of his cases (1,630 c.c. during twenty-four hours).

John M. McCoughan, St. Louis: **Pancreatic Fistula: Clinical and Experimental Observations.**—Six cases of pancreatic fistula were reported, 2 of which resulted from external trauma, 3 from injury at operation, and 1 from acute pancreatitis. In 1 case the fistula was transplanted to the stomach with a successful result. In 3 cases the fistula closed spontaneously. Irradiation of the pancreas by x-ray was tried in 1 case, but it did not cause the fistula to close. Observation showed that, although there was an increased flow following the intake of water, peptone, and protein, a fatty meal produced the greatest increase in secretion from the fistula. Glucose and atropine decreased the secretion, and epinephrine stimulated the flow.

Frank L. Meleney, New York City: **The Historical Aspects of Surgical Infections.**—Meleney reviewed the history of surgical infections from antiquity up to fifty years ago. The prevention of putrefaction was studied before its cause was known. The use of carbolic acid as an antiseptic was suggested by the fact that it deodorized the sewerage of certain towns in England. In 1867 Lister stated that for six years he had taught that bacteria was the cause of suppuration. In 1881 the principles of Lister were accepted in England, but in 1882 the majority of the members of the American Surgical Association were still anti-Listerian. No detailed description of hospital gangrene is to be found in Lister's publications apparently because it was so common and everyone was so familiar with it that a description was considered unnecessary. Hospital gangrene appears to have been used to describe various degrees of acute and chronic infections. Meleney thinks that bacteriology in surgery has not had the attention it should have from surgeons.

Waltman Walters, Rochester, Minn.: **Carcinoma of the Stomach.**—The author reviewed all the cases of carcinoma of the stomach seen at the Mayo Clinic since 1908. Twenty-five per cent of all cases gave an ulcer type of history. Eighty per cent had been treated previously by medical regimen for ulcer with relief. Considering those cases in which resection was carried out, 75 per cent gave positive x-ray evidence of carcinoma, 10 per cent were reported as benign ulcer, and 11 per cent were found to be operable after being reported inoperable by x-ray examination. Fifty-eight per cent of the total number were operated upon, 45 per cent were just explored, and 26 per cent of the total were resected. There was an average mortality of 16 per cent in all resected cases. Twenty-five per cent survived ten years; 15 per cent, fifteen years; and 10 per cent were living twenty years after operation. A significant finding was the fact that, when the survival curve for these patients was plotted, it was parallel after six years with the expected mortality curve for the same age, indicating that a patient who has survived six years after resection for carcinoma of the stomach rarely has a recurrence. Walters wished to emphasize that a high percentage of cases present typical ulcer histories and that only a short medical test period (three weeks) should be used.

E. Eric Larsen, Los Angeles: **230 Patients Subjected to Gastric Resection by 50 Surgeons.**—A study of the records of 230 patients from three hospitals on whom a partial gastrectomy had been done by fifty surgeons was reported. The diagnosis was carcinoma in 89, duodenal ulcer in 46, gastric ulcer in 70, and recurrent or previously operated cases, 31.* Reichel-Polya procedure was done in 117, Balfour-Polya in 34, Hofmeister-Finsterer (post.) in 26, Hofmeister-Finsterer (ant.) in 5,

*These figures are only approximately correct, probably due to the reviewer's error.

Billroth I in 34, Billroth II in 18, sleeve resection in 7, and total resection in 7 cases. The mortality for the series was 33 per cent. The mortality for resection in duodenal ulcer was 24 per cent. Larsen stated that the highest mortality followed operations by surgeons of inadequate experience and training. Since his study had been reported in staff meetings of the three hospitals, the mortality has decreased to 9 per cent.

Arthur R. Metz, Chicago: **Obstruction of Stomach Due to a Congenital Mucosal Cyst.**—The case reported is the only one in which two complete septa have been found. No similar case is reported in the literature. One septum was prepyloric and the other midgastric. The patient was a Jewish male infant. Continuous vomiting was present and a mass could be felt. At operation, after the cyst was entered, openings were made in the stomach proximal to the upper septum and in the duodenum below the lower septum. There was no tract around the cyst. Radial incisions were made in the septa and a catheter was left in the duodenum for feeding purposes. Microscopic sections through the septa demonstrated normal mucosa. A gastrointestinal series disclosed a normal stomach and duodenum three years later.

Erwin R. Schmidt and **F. E. Mohs,** Madison, Wis.: **The Chemosurgical Treatment of Cancer, a Microscopically Controlled Method.**—The authors described a method of removing cancer under what they term microscopic visualization. It is made possible by using a technique for producing a fixation of tissue in situ, by the application of zinc chloride, so that when excised the base of the mass may be studied serially under the microscope. Areas that are positive are again treated with zinc chloride, removed, and studied microscopically until an entirely noncancerous layer is obtained. They reported 440 cases which were so treated and which were followed for from one to four and one-half years with 93 per cent free of recurrence at the site of the primary lesion. They point out that, regardless of the grade of malignancy, this treatment can be used.

Vernon David, Chicago, stated that, although chemotherapy has been used for ages and has been condemned by the medical profession, this method should be given a trial under the strictest conditions and reported on at a later date.

James F. Percy, Los Angeles: **Advanced Cancer of the Nose and the Accessory Sinuses; Treatment by Actual Cautery.**—Percy gave a description and showed pictures demonstrating his technique used in treating advanced cancer of the sinuses. Entrance into the maxillary sinus was made through a U-shaped incision over the sinus. The malignant growth was destroyed by actual cautery. He showed some cases in which it was necessary to extend through the dura into the brain tissue. For the prevention of meningitis he left a charred sponge closely adhering to the dura or brain tissue.

Carl E. Black, Jacksonville, Ill.: **Three Thousand Appendectomies.—James F. Percy,** Los Angeles, read Black's paper concerning an analysis of 3,315 appendectomies by the staff of Passavant Memorial Hospital, Jacksonville, Ill., which represented the work done in one small hospital by many surgeons. The first part of the period (1923-1931) showed a mortality of 5 per cent compared to a 4.48 per cent mortality for the second period (1931-1939). The mortality varied considerably according to the individual surgeon. Operator U. had a mortality of 6.8 per cent in 831 cases in contrast to Operator W-I's 0.7 per cent mortality in 274 cases. In seeking a reason for a higher mortality in the first period, the following were considered important: delay in diagnosis, delay in treatment, and inadequate pre- and postoperative treatment. Multiple surgery at the time of appendectomy was considered

very important, evidenced by a mortality of only 2 per cent when only the appendix was removed.

Raymond W. McNealy and **Manuel E. Lichtenstein** (by invitation), Chicago: **Strangulated Femoral Hernia Sac Without Abdominal Contents.**—The authors stated that the contents of a femoral hernia should be expected to become strangulated in a rather considerable number of cases, but that strangulation of the sac alone was infrequent. They reported 10 cases occurring in a series of 401 cases of femoral hernia. They discussed the anatomy of femoral hernias and explained that trauma to a femoral sac may cause inflammation with obliteration of the neck and accumulation of fluid within the sac. Thrombosis and edema then will produce strangulation. A history of trauma accompanied with pain in the groin and a tender discolored mass suggest this condition.

Stuart H. Harrington, Rochester, Minn.: **Diagnosis and Treatment of Substernal Types of Diaphragmatic Hernia.**—Harrington reported 4 cases of substernal hernia occurring in a series of 270 cases of various types of diaphragmatic hernia. This space, the foramen of Morgagni, was described as a weak region, and probably these hernias are not traumatic in origin, since none gave a previous history of injury. Their anterior position as shown on the x-ray film would immediately classify them as substernal, although the x-ray films might suggest tumor. Two of the cases had been previously diagnosed as tumor and not until exploration was the true condition found. An upper abdominal approach is the one of choice.

Warren H. Cole and **R. D. Weber**, Chicago: **Surgical Considerations in Constrictive Pericarditis.**—Three such cases were reported, 2 of which were operated upon. In 1 of the operated cases the results were good after a rather prolonged convalescence. The other case developed severe myocardial decompensation and died postoperatively. Diagnosis may be confused with cardiac failure and cirrhosis of the liver. First the patient complained of general weakness, dyspnea on exertion, ascites, and edema of the extremities. The electrocardiogram showed an eversion or flat T-wave. There was a high pulse pressure, circulatory delay, a blood volume above normal, and a low cardiac output. A small heart shadow with restriction on the right and left side is very significant. There is a 30 per cent mortality from operation, and, although the results are good, recovery is slow.

Stuart Harrington, Rochester Minnesota, in discussing Cole and Weber's paper, stated that too much emphasis on a small heart may lead to difficulty, and demonstrated cases with normal-sized hearts. Also, he thought it extremely important that 7 out of 9 cases at the Mayo Clinic presented areas of calcium deposit as seen on the x-ray film and at operation.

Loyal Davis and **John Martin**, Chicago: **The Surgical Problem of Unilateral Exophthalmos.**—Martin presented the paper, confining his remarks to those cases caused by tumors and arteriovenous aneurysms. He stated that the intracranial tumors most commonly found were meningiomas of the greater wing of the sphenoid, which at times were extremely vascular and difficult to manage. When due to meningiomas, pulsating exophthalmos is not present nor are superficial dilated veins necessarily seen. Cranial nerves most commonly involved are the third, fourth, and sixth. The x-ray findings are generally very helpful. An enlarged optic foramen is caused by glioma of the optic nerve as well as by meningioma, but there is an absence of bone erosion in the former. In the aneurysmal cases one sees the characteristic pulsating exophthalmos with a bruit, a thrill, and a dilatation of the peripheral

veins. The cause of the exophthalmos is thought to be due to a reversal of blood flow in the ophthalmic vein with stasis and hyperplasia of the orbital contents. There are no x-ray changes seen in cases of aneurysm. Treatment of tumor cases consists of a transfrontal excision which may be difficult due to vascularity. In arteriovenous aneurysms ligation of the common and external carotid arteries is the procedure of choice, although sometimes it is necessary to ligate the internal carotid intracranially, distal to the aneurysm.

Frank R. Teachenor, Kansas City, Mo., described 1 case in which he used a lateral approach to remove a meningioma and reported 3 cases of aneurysm. **Alfred W. Adson,** Rochester, Minn., showed 1 case in which the internal carotid was ligated intracranially and the ophthalmic artery obliterated with a silver clip, because there had been a recurrence after previous ligation of the carotid artery in the neck.

James Barrett Brown and **Frank McDowell,** St. Louis: **The Late Functional Results Obtained by the Free Skin Grafting of Burns.**—Brown showed by motion picture films his remarkable results in severe burns, especially on the neck. After extensive excision of scar tissue from the neck, full thickness grafts were obtained from the abdomen and in numerous cases the whole front of the neck was restored with one graft. The donor site was covered with a split graft from the thigh.

Earl Padgett, Kansas City, Mo., discussed Brown's paper, stating that he is using the calibrated skin grafts almost entirely and feels that his results are much better and that much time is saved.

Verne C. Hunt, Los Angeles: **Hemangioma of the Large Bowel.**—Hunt reported a case of hemangioma involving the entire rectosigmoid, the rectum, and the uterus treated by a two-stage (Lahey) abdominoperineal resection and hysterectomy, with excellent results. The patient's symptoms of bloody stools with an occasional massive hemorrhage and secondary anemia dated back twenty-one years. Hunt stated that 48 cases had been reported, 20 involving the colon and 28 involving the rectum. These varied from small capillary nevi to cavernous hemangioma.

Everett P. Coleman, Canton, Ill.: **Recurring Jejunal Intussusception.**—The rarity of the condition was discussed by Coleman, who estimated that jejunal intussusception occurs in about 0.9 per cent of all intussusception cases. He discussed the general symptoms and classifications of intussusception and proceeded with the history of his case, which was of six years' duration. The patient had attacks of abdominal pain, nausea, and vomiting, which became more frequent. Barium studies failed to disclose the lesion present. Transnasal duodenal suction was used in preparation for surgery. At operation a large blue mass was found beginning 10 cm. below the ligament of Treitz. It was resected and an end-to-end anastomosis was done. The intussuscepted bowel consisted of nine layers and measured 6 feet, 10 inches in length.

Jay Ireland, Chicago: **The Treatment of Intussusception.**—The 133 cases occurring in the Children's Memorial Hospital, Chicago, from 1920 to 1940 were divided into two ten-year periods. The first period revealed a 41 per cent mortality in 54 cases as compared to a 22 per cent mortality in the 79 cases of the second group. Ninety-one per cent were diagnosed within the first twenty-four hours, 22 per cent within the next twelve hours, 8 per cent the next twelve hours, and 27 per cent over seventy-two hours. In 92 per cent vomiting occurred. In 49 per cent bloody stools

were present, and a mass was felt in 72 per cent. Farr manipulation was done in all cases (air inflation with belly open) and it was successful in 83 per cent. Two cases were operated upon by the technique of Montgomery. In 4 cases excision was done, 3 with lateral anastomosis and the other with end-to-end anastomosis. Ileostomy was done in 3 cases followed by death. Ireland proposed a new procedure which consisted of injecting glycerin between the intussuscepiens and intussusceptum followed by gentle manipulation of the finger between the two. Two severe cases have been reduced in this manner.

Edwin M. Miller, Chicago, discussed the papers on intussusception, and stated that only when more cases are treated by the procedure described by Ireland (glycerin injection and manipulation) could its value be ascertained. In his own 58 cases 19 were extremely difficult to reduce. In 10 it was impossible to reduce the intussusception. Five of this group recovered after extensive resection (exteriorization). He advised placing patients on their abdomen until ready to close the ileostomy. **Stanley J. Seeger,** Milwaukee, Wis., discussed 60 cases from the Milwaukee Children's Hospital which showed a 33 per cent mortality, although there has been a decrease in late years. The decrease, he thought, was due to better pre- and postoperative treatment and the fact that all cases are now having immediate operation. **George Packard,** Denver, Colo., reported cases from the Denver Children's Hospital, with the remarkably low mortality of 6.6 per cent in the last five years. Considerable influence in keeping this mortality rate low was thought to be due to the use of postoperative suction.

Frank C. Mann, Rochester, Minn.: **Experimental Studies in Motor Mechanism of the Intestine.**—Different types of exteriorized bowel loops were discussed and the importance of a loop covered by skin was emphasized. Different levels were studied. Alvarez's theory was demonstrated in that higher segments of bowel show a greater rate of activity and the rate is decreased progressively as the cecum is approached. Definitely increased motor function followed feeding and was not affected by section of the vagus. There was a definite decrease on fasting. Liquid food increased activity, but activity was more marked and lasted longer with solid foods. Peritoneal irritation (Lugol's solution as irritant) inhibited motor activity, but not after both splanchnics were severed. Motor activity was not affected by gall bladder distention. Cascara affected activity very little, but magnesium sulfate produced a marked disturbance of all activities. Ether and operative exposure caused almost a complete secession of motor activity for about four hours. Activity decreased after enemas.

Charles Puestow, Chicago, stated that he had had an opportunity to study a human bowel loop covered by skin and it had reacted the same as does that in the dog.

Maurice Kahn, Los Angeles: **Surgical Treatment of Ulcerative Colitis.**—Kahn described the pathology of this disease, citing as complications perforation, abscess and fistula, hemorrhage, stricture, and, rarely, thrombophlebitis. He said that polyposis occurred in 13 per cent, which tended toward carcinomatous degeneration. Ninety-five per cent of the cases finally showed extension to the ileum. He felt that about 25 per cent of the cases were surgical. Ileostomy should be used at times in the acute fulminating type and the results and mortality would be much better if used earlier. Cecostomy and appendecostomy were found to give poor results. In the chronic intractable type complete colectomy should be used before the previously stated complications occur. Six cases were reported. In 2 ileostomy

was done, in 1 an ileo-sigmoidostomy, and in 3 total colectomies. The second stage had just recently been done in another case.

In discussion, **Frank Meleney**, New York City, reported good results by the use of zinc peroxide (10 per cent) in polyvinal alcohol (2 per cent) for irrigations. Best results were obtained when fed through a cecostomy.

William J. Carson, Milwaukee, Wis.: **Transplantation of Fascia Lata in Cystopexy.**—A case was reported which had a complete prolapse twenty-one years following a total hysterectomy. A free graft of fascia lata was cut to fit the pubic arch, being anchored to the symphysis pubis, the descending ramus of the pubis, the ramus of the ischium, the tuberosity of the ischium, and the base of the broad ligament on each side. The results were good four and one-half years post-operatively.

REVIEW OF THE SOUTHERN SURGICAL ASSOCIATION MEETING, DEC. 10, 11, 12, 1940, HOT SPRINGS, VA.

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THE annual meeting of the Southern Surgical Association was held Dec. 10, 11, and 12 at the Homestead Hotel in Hot Springs, Va. Of a total of forty listed papers, thirty-eight were presented.

1. **Grover C. Penberthy,** Detroit, Mich.: **Chemotherapy as an Aid in the Treatment of Osteomyelitis.**—Statistics show a lowering of the incidence of osteomyelitis in recent years, possibly the result of improved nutritional status in the underprivileged class. The present report is based on nineteen cases, with treatment and conclusions as follows: Sulfanilamide is not effective in staphylococcal infections. Sulfapyridine, along with blood transfusions, gave encouraging results. Sulfathiazol, although not more effective, was found to be better tolerated than sulfapyridine, and for this reason is preferred. Even though high blood concentration levels were maintained, untoward results from sulfathiazol were not frequent or serious. One and one-quarter grains per pound of body weight were given over a twenty-four-hour period at four- to five-hour intervals, and the dose reduced as clinical improvement occurred. Large initial doses were not given. Recently, following saucerization in chronic osteomyelitis, cavities have been packed with sulfathiazol powder. The value of local use of the drug in compound fractures was referred to. Of the author's cases, 50 per cent had positive blood cultures, most frequently staphylococcus, but, in some instances, hemolytic streptococcus. Chemotherapy has considerably reduced the period of hospitalization, as well as the incidence of secondary or metastatic abscesses. None of the author's cases had involvement of other bones after chemotherapy was started. Deformities as well as mortality have been reduced by this form of treatment.

Discussion: **Frank D. Dickson,** Kansas City, Mo., cited his experience with chemotherapy in twelve cases of osteomyelitis, some of which were acute. In addition to early operation he placed sulfathiazol powder into the wounds, which were then closed. The drug was also given for twelve days by mouth. All healed, with no mortality.

2. **Frank D. Dickson,** Kansas City, Mo.: **The Surgical Treatment of the Arthritic Patient.**—This presentation was in the form of a moving picture accompanied by remarks by the author. The persistent deformities which constitute economic and emotional adjustment problems were discussed. Of the approximately 1,000,000 cripples in the United States, some may be relieved by surgery. Surgical intervention may be indicated for: (a) incapacitating disability and (b) removal of a focus which is propagating the disease. It was emphasized that an infected synovial membrane may act as the focus of infection. In twenty-six cases in which synovectomy was performed, twenty-two cases were definitely relieved. In rheumatoid arthritis the operation must be delayed until the quiescent stage; whereas, in hypertrophic arthritis operation can be done at any time, because there

is no acute phase. In addition to the moving picture illustrating synovectomy, other surgical procedures, i.e., manipulation, capsulotomy, arthroplasty, and arthrodesis, were illustrated and discussed. The use of a vitallium cap in hip arthroplasty was referred to.

Discussion: **Charles S. Venable,** San Antonio, Tex., elaborated on the use of vitallium caps in arthroplasty. He described a cap which has been devised for the head of the radius, and another employed in knee arthroplasty. **Paul B. Magnuson,** Chicago, discussed the effect of repeated trauma, caused by arthritic excrescences, in the full evolution and maintenance of both destructive or rheumatoid arthritis, and hypertrophic arthritis. He has done joint débridement in 62 cases, removing rough and thickened tissues. All cartilage is removed down to bare and bleeding bone. Any ridges caused by removal of cartilage should be parallel to the direction of motion. The results in his cases have been astonishing.

3. **Lieut.-Col. William C. Munly,** Washington, D. C.: **Notes on Medical Service in the Present Mobilization.**—The manifold medical problems involved in present-day mobilization, and the plans which have been made for their solution, were outlined. These problems were divided into two main categories; i.e., (a) the provision of adequate medical service and (b) the training of enlisted men. Plans for initial as well as for expanded hospital facilities, and for medical and nursing personnel, were discussed. Appreciation was expressed for the cooperation of various societies, universities, and other bodies which are concerned in the plan. Dental, veterinary, medical administrative, sanitary corps, and medical department enlisted personnel requirements were presented. The organization and function of enlisted specialists, i.e., laboratory, dental, sanitary, x-ray, surgical, veterinary, and pharmaceutical, was reviewed. The supplying of technicians has been undertaken by the Red Cross. Males not physically qualified for military service, as well as females, may serve in a number of civilian capacities. Station hospitals, with a total bed capacity of 68,000, will provide for 5 per cent of the military population. General hospitals, with a total bed capacity of 14,000, will provide for an additional 1 per cent of the military population. Reserve depots for medical supplies have been provided. The organization and activities of the National Health and Medical Committee were outlined. The National Research Council facilities have been made available, and at present there are seven main committees actively functioning; i.e., the committees on chemotherapy, medicine, surgery, aviation medicine, transfusion, surgical specialties, and neuropsychiatry. There is also a committee on information, and many subcommittees.

Discussion: **Charles Mixter,** Boston, discussed the care of serious casualties in advanced areas. Many cases of head, chest, and abdominal injuries are detrimental to military operations and should not be operated upon at advanced hospitals. Civilian surgeons are likely to be forgetful or to overlook the importance of operating upon a greater number of minor cases instead of expending fruitless efforts and consuming an unwarranted amount of time in operating upon hopelessly wounded cases. The transportation of the injured to base hospitals by means of commercial airplanes, the use of autogiro planes, and the use of the many presently existing landing fields, golf courses, and lakes, for the landing of planes was discussed. **Harvey Stone,** Baltimore, also emphasized the importance of speed in returning men to active duty. Attention should be given to the great number of relatively minor injuries rather than focusing attention on the seriously wounded individuals. Stone felt that the injured men would get better attention if they were transferred 200 to 300 miles behind active battle zones. He felt that the failure

of England and France to make a better showing in the present war in Europe was due to their neglect in the use of the most modern types of transportation. **J. M. T. Finney, Sr.**, Baltimore, reflected on the woeful unpreparedness of the United States at the time of its entry into the World War of 1914-1918 and was impressed by present plans for preparation. He said that had it not been for efficiency, self-denial, and consecration in the last war on the part of the medical corps personnel, soldiers would not have fared so well. **Raymond T. Sullivan**, New York City, echoed Finney's remarks and lauded the work which is being done in the education of the medical personnel. **Arthur Shipley**, Baltimore, agreed with Mixter in regard to the military importance of caring for great numbers of relatively minor casualties rather than devoting much time to the hopelessly injured cases. He cited the fact that there is at present no communication zone; everything is combat zone. The mobile hospital unit which has been tried in peacetime maneuvers, he felt, would be suitable for use close to combat zones.

4. **Irvin Abell**, Louisville, Ky.: **Medical Preparedness.**—Abell reviewed the work on military preparedness being done by the American Medical Association. He discussed the need for supplying qualified physicians to industry, and referred to the need for assuring adequate care of civilian population while at the same time supplying the personnel required for military service. The provisions of the selective service act were considered, including that desirable feature whereby deferment might be obtained to avoid interfering with the training of men for future military or civilian requirements. Medical men within the draft ages, he felt, should apply for a reserve officer's commission, as otherwise they might have to do preliminary service as an ordinary enlisted soldier. The work of the National Defense Council and the Health and Medical Committee was outlined.

5. **Alfred Blalock**, Nashville, Tenn.: **Blood and Blood Substitutes in the Treatment of Shock.**—In secondary or hematogenic shock, associated with reduced blood volume, blood and blood plasma are of great value in treatment. Salt solution infusions are unsatisfactory because not only does the salt solution leave the circulation, but blood proteins are carried out also. When plasma, blood, or serum is used in the presence of increased capillary permeability, such a marked outpouring of blood proteins does not occur. For blood transfusion the vacuum bottle method was considered superior, because of its simplicity and because contamination can easily be avoided. In discussing the use of plasma, Blalock said that, although hemoconcentration is usually present in shock, the bad effects of hemoconcentration have been overestimated, especially if blood volume is maintained. A given quantity of plasma causes a greater increase in osmotic pressure than does an equal quantity of whole blood. Plasma can be stored more easily than can whole blood and the danger of reaction is less, especially if the plasma is pooled in order to decrease the concentration of agglutinins. Methods for the preparation of clear dilute plasma and dried plasma were described. Some workers prefer dried serum, while others believe that liquid plasma and dried serum are equally good. The preferences of various armies in respect to blood or blood elements were cited; i.e., the Russian army uses whole blood, the German army uses whole blood from universal donors only, the British army prefers liquid plasma.

Discussion: **Roy D. McClure**, Detroit, discussed a method for concentrating blood or plasma. It was found that, when blood is placed within a cellophane container, the volume of the blood is decreased, and it occurred to Hartmann that this method could be used for concentration of plasma. By this method, dry plasma can be rapidly produced. It is possible to produce dried plasma in four

hours by this method; whereas, other methods require forty hours. The dried plasma is stored in the containers used for the drying process. McClure stressed the importance of keeping the dried plasma in moisture-proof containers in order to avoid gumminess of the plasma. **Waltman Walters**, Rochester, Minn., advocated the collection of blood from recruits and civilians in anticipation of war needs. He also discussed the advisability of indicating the blood group of each soldier on his name plate, and referred to the transportation of casualty cases by airplane. **Bradley L. Coley**, New York City, relayed English opinions in regard to blood transfusion; i.e., a preference on the part of some for dried serum because it keeps indefinitely and it does not become contaminated with bacteria. He reported that the British are using from four to six pints of plasma per case.

6. **I. A. Bigger**, Richmond, Va.: **Peripheral Vascular Injuries.**—Bigger considered it important that practice in arterial suture in an animal experimental laboratory should precede the execution of this type operation upon human beings. He discussed the effects of spontaneous shifting of tissue planes in effecting hemostasis. Operations on arteries should be avoided in the presence of infection. Many pulsating hematomas heal without operative intervention, and for this reason not all pulsating hematomas demand immediate operative exploration. When the circulation in a limb distal to a pulsating hematoma is good, operation may be delayed. Direct suture is ideal if there is no devitalized area around the site of injury, but this latter condition frequently does not exist because in modern warfare many of the injuries are produced by high explosive shells. Venous transplants have not proved successful. The local application of sulfonamide drugs in contaminated wounds was advised in order to reduce the degree of infection. Regional heparinization was advocated and it was reiterated that silk should be employed for sutures. The following methods for the prevention of gangrene following ligation of important arteries were discussed: (a) sympathetic nerve block by novocain, before and after operation in elective cases, and following operation in the emergency cases; (b) prevention and control of infection; (c) occlusion of concomitant veins at the same level or proximal to the point of arterial ligation; (d) rest of the extremity after occlusion, with the limb placed on a level at which the veins are maximally filled; (e) avoidance of pressure; (f) maintenance of temperature at normal levels, with particular precaution in respect to the application of external heat; (g) passive vascular exercise by means of the glass boot for the application of alternating positive and negative pressure to the part was considered to be contraindicated in many cases; (h) restoration of blood volume and red blood cell content by means of transfusion; (i) the administration of oxygen by inhalation; (j) the administration of nicotinic acid; (k) the administration of papaverine for whatever good effects this drug may exert.

Discussion: **John W. Price, Jr.**, Louisville, Ky., did not share the enthusiasm in regard to the possibility of being able to suture vessels under conditions of war practice. During the war of 1914-1918, however, he did frequently have occasion to ligate arteries. He recommended ligating concomitant veins. **Deryl Hart**, Durham, N. C., discussed the importance of ligating arteries both proximal and distal to points of injury. **Alton Ochsner**, New Orleans, La., felt that, in order to obtain full benefit from sympathetic nerve block for the prevention of gangrene following arterial ligation, this procedure should be done as early as possible. Ochsner referred to the successful ligation of the common iliac artery by Mims Gage, New Orleans, for a mycotic aneurysm, the success of the procedure being considered largely due to the preliminary blocking of the lumbar sympathetic

nerves. Ochsner felt that embolectomy for arterial embolism is no longer necessary, as the gangrene resulting from embolism is due to distal spasm, and this may be successfully relieved by sympathetic block. Incidental comment was made in respect to the value of sympathetic block in the treatment of thrombophlebitis and phlebothrombosis. **John C. A. Gerster,** New York City, advocated that, in order to avert disastrous results from secondary hemorrhage, which is likely to occur between the seventh and the tenth days following arterial injuries, a loose tourniquet be kept around the limb, proximal to the sites of infected amputation stumps.

7. **Parke G. Smith,** Cincinnati, Ohio: **Urologic Surgery.**—Although no reports are yet available concerning urogenital injuries which have occurred in the present European war, a consideration of the character of present warfare makes it possible to anticipate certain things which might be expected. Previous experiences and reports reveal that 65 per cent of bladder injury cases died. The mortality in kidney injuries was 20 per cent, and even 2.5 per cent of those with wounds of the external genitals died. The importance of prompt evacuation to base hospitals of bladder or urogenital casualty cases was discussed. The differences in the present and the last World War were alluded to, especially in respect to the fact that at present there are many injuries to civilians. Injuries in modern warfare are most frequently due to crushing forces rather than to penetration and resemble the injuries which are caused in automobile accidents in civil life. In discussing the management of renal injuries, it was considered that in the instance of minimal or moderate injuries conservative treatment should be employed; when actual renal parenchymal damage has been done, exploration should be done, clots removed, and the kidney sutured; in the extremely severe injuries nephrectomy must be done. Smith referred to the increased number of bladder ruptures due to distention of the bladders of occupants of air-raid shelters, where both sexes commingle. Chemotherapy has greatly improved the outlook in respect to the control of infection following urologic injuries.

8. **Daniel C. Elkin,** Atlanta, Ga.: **Injuries of the Chest.**—The narrow margin of safety under which thoracic viscera functions makes thoracic injuries extremely serious, and such injuries are likely to be rapidly fatal. The management of chest wounds includes the treatment of shock, the treatment of hemorrhage, and the restoration of cardiorespiratory physiology. Pleuropulmonary wounds may be open or closed. The open wounds are much more serious and should be débrided and closed. The closed wounds are less serious, and treatment should usually be conservative, except in the instance of heart wounds. Depressed rib fractures sometimes require elevation under anesthesia. Block of the intercostal nerves, for the relief of pain, may be tried for the possible benefits which this procedure may afford. The methods for managing the following complications were discussed: pneumothorax, atelectasis, prolapse of the lung, empyema, hemothorax, traumatic asphyxia, ileus, and subcutaneous as well as mediastinal emphysema. Crushing injuries of the chest due to automobile accidents were discussed, with special reference to contusion of the heart caused by impingement against the steering wheel. In the latter type of injury the sternum and ribs may not be fractured. The treatment is entirely symptomatic. Approximately 2 per cent of wounds of the chest are associated with penetrating wounds of the heart. Attention was drawn to the importance of the rise in venous pressure and the fall in arterial pressure as indicators of cardiac tamponade. Intercostal thoracotomy, with removal of part of the sternum, was considered to be probably the best approach to heart wounds. The pericardium should be loosely closed.

Discussion: **Albert O. Singleton,** Galveston, Tex., made the interesting observation that the relative incidence of gunshot and stab wounds is related to the economic status of the negroes. In good times, when firearms are possessed, gunshot wounds are more common; whereas, in poor times, stab wounds are more frequent. At present, bullet wounds are more frequent. Singleton advocated avoidance of entering the pleura when it has not been perforated, but said that it is important to enter the pleural cavity when it has already been perforated. **Deryl Hart,** Durham, N. C., discussed what was best to do in cases, seen two to four weeks after injury, in which there is an infected hematoma. In his experience he encountered difficulty in attaining satisfactory re-expansion in such cases. **I. A. Bigger,** Richmond, Va., stated that decision in regard to the proper handling of hemothorax is sometimes difficult. When the amount of blood in the pleural cavity is large, it should be aspirated, not only to relieve pressure, but also to obtain blood which may be employed for autotransfusion, if the case is seen within the first few hours following injury. When the amount of hemothorax has been large, air replacement is advisable. Bigger expressed the belief that aspiration may be employed to advantage in cases of heart wound tamponade, either as a preliminary procedure or as a definitive treatment, especially in military practice.

In closing, Elkin agreed that he, too, had encountered cases with infected hematomas in which it was difficult to obtain a cure. In 1,500 cases of chest wounds studied by him, there has been only 3 per cent of infection. He believes that infection would be higher if all cases were aspirated or drained. Increased intrathoracic pressure or definite infection, he believes, should be the only indication for aspiration of the pleural space. Elkin did not agree that aspiration should be done in cases of heart tamponade, as it is impossible to select the cases in which this will be sufficient.

9. **Vilray P. Blair,** St. Louis: **Plastic and Facial Maxillary Aspects of Military Surgery.**—The plans which were made by the Surgeon-General for the management of face and mouth injuries in the World War of 1914-1918 were reviewed. Many faciomaxillary injuries are at once fatal. In the nonfatal cases such injuries may exert a very harmful effect on the morale of the injured individual, who may cause much expense to the government in compensation claims. For the best management of faciomaxillary injuries, it is oftentimes advisable to pair a dentist with a general surgeon. The importance of proper early treatment of these individuals was emphasized in order that long periods of disability and tedious multiple operations might be averted. Blair warned against the removal of any detached bone and advocated its early replacement. In the instance of wounds about the mouth in which there has been loss of considerable substance, suture of the mucous membranes of the skin, as recommended by Tuffier, is a very good procedure. Scrubbing out of particles of black oil, and picking out with a knife of black powder, at the site of burns shortly after injuries in which these substances have been implanted into the skin will prevent subsequent tattooing.

Discussion: **Robert Ivy,** Philadelphia, emphasized the fact that plastic surgery has broad aspects and is not limited to facial injuries. He agreed that cooperation with the dental surgeon is necessary for the proper management of many faciomaxillary injuries. He stressed the following elements in the management of these cases, i.e., arrest of hemorrhage, establishment of a proper airway, temporary fixation of jaw fractures before an attempt is made to close the wound, provision for safe transportation, including the placing of the patient in a face-down position on a litter. Apparatus was demonstrated which has been devised for bringing the upper or lower jaw forward. Such apparatus can be improvised by using tongue blades or wire coat hangers.

10. **Guy A. Caldwell,** New Orleans, La.: **New Developments in the Treatment of Compound Fractures.**—Although methods for treating these injuries have varied within recent years, the basic principles remain the same. Advances include better methods for the treatment of shock, chemotherapy, roentgentherapy, better operating equipment, and the use of pectin-sulfathiazol jelly. Among 300 cases at the Charity Hospital in New Orleans, there were only twenty potentially infected cases. This observation was introduced to indicate how reports on chemotherapy and roentgen therapy might be misleading in respect to the value of these agents. It was advocated that bone fragments should be withdrawn into the wound when traction splints are applied in preparation for transportation of the patient. Present improved methods for treatment of shock permit earlier débridement and assure better circulation, and there are fewer serious wound infections. The treatment of shock, if possible, should be done in the operating room. Caldwell felt that tetanus toxoid immunization will replace the administration of tetanus antitoxin. He considered gas gangrene antitoxin of doubtful prophylactic value. In discussing the preparation of the patient for operation, he deprecated the employment of soap and water and advocated the use of ether and iodine. Meticulous dissection is superior to irrigation of the wound. Instillation of strong antiseptics into the wound is undesirable. The limb should be adequately immobilized during the period of preparation as well as during operation. In Spain and Finland most wounds were left open and the incidence of gas gangrene was extremely low. Joint wounds, however, should be sutured. Lacerations over subcutaneous bones should be sutured, but counterincisions should be made. Internal fixation should be employed only in carefully selected cases. Adequate immobilization with provision for access to the wound was considered superior to encasement in plaster. The use of pectin-sulfathiazol jelly has yielded very gratifying results. It not only eliminates odors, but favors healing. In order to anticipate the development of gas bacillus infection in compound fracture cases, tissue obtained in the course of débridement should be sent to the pathologic laboratory. Zinc peroxide paste may be employed to advantage in some cases. In discussing x-ray therapy for gas bacillus infection, the author did not believe that it alone is of definite value, but he thought that it might exert an inhibitory action under some circumstances.

11. **Mont R. Reid** and **B. N. Carter,** Cincinnati, Ohio: **Traumatic Surgery.**—Reid limited his comments to the treatment of fresh traumatic wounds. He felt that this type of surgery is more exacting than many types of elective surgery which are generally considered of greater magnitude. The principles of hemostasis, débridement, and rest were re-emphasized. Antiseptics were considered harmful. A good blood supply should be maintained, both in respect to amount and quality of the blood. Healthy cells have a remarkable power to combat bacteria, and healing of wounds is brought about by growth and activity of living cells. Early assay and treatment of shock are important. The author discussed in detail: (a) management of simple incised wounds, (b) delayed closure of infected wounds, (c) treatment of contaminated lacerated wounds, and (d) infected traumatic wounds. In the instance of infected traumatic wounds tendons and nerves are not sutured primarily. The wound is packed open with vaseline and plaster fixation is afforded. The author believes that a window should not be cut in a plaster cast because herniation due to edema is likely to result at the site of fenestration. If a dressing must be done, he felt that the entire cast should be removed.

Carter showed slides illustrating the types of wounds and their treatment, as discussed by Reid.

12. **C. C. Coleman,** Richmond, Va.: **War Wounds of the Nervous System.**—Information is not yet available in regard to the present war injuries of the nervous system. Injuries of the nervous system were classified. Improved results in the management of these injuries must depend on elimination of delays and institution of treatment and in the standardization of the methods of treatment. The serious associated injuries frequently present in modern war injuries are responsible for many of the fatalities. Prompt evacuation and transportation, even by airplane, would be helpful in reducing the morbidity and mortality associated with nervous system injuries, but it should be borne in mind that patients with open wounds of the skull do not tolerate altitudes above 5,000 feet. Delayed complete treatment at a base is better than treatment at advanced posts, unless the facilities at the latter are unusually good. The employment of suction apparatus and electrosurgical units in the débridement of brain wounds was discussed. At times, head injury cases may be operated upon to advantage as late as forty-eight hours following injury. Unsutured scalp wounds at times may be packed with vaseline. Coleman felt that no attempt at chemical disinfection by means of antiseptics should be made. In the instance of spinal cord injuries, associated abdominal injuries or urinary tract infections frequently are responsible for death. The hopelessness of many spinal cord injuries was discussed; in many such cases operation must consist entirely of removing foreign bodies and affording drainage of infected areas in the overlying soft parts. In the management of bladder paralysis, suprapubic cystotomy is the treatment of choice, especially in war practice. Peripheral nerve injuries constituted 4.5 per cent of all casualties in the past war. Many of these cases were operated upon late, and recovery of function was very incomplete in most instances. The employment of chemotherapy for the purpose of retarding or preventing infection offers encouraging possibilities, and results at present should be better than in the World War of 1914-1918. Primary nerve suture should be done whenever possible. Autogenous nerve grafts were unsuccessful in the last war in all cases the author had an opportunity to observe. The use of fibrin as a means of maintaining nerve approximation was mentioned, but Coleman felt that the use of this substance is obviously limited to those cases in which the nerve ends can easily be approximated.

Discussion: **John S. McEwan,** Orlando, Fla., stated that he was active in a large hospital in France during the World War of 1914-1918. Although he did many nerve sutures, he did not have an opportunity to follow them up. He considered pieces of clothing as important causes of infection, and emphasized the importance of removing these in performing débridement.

13. **Ambrose H. Storck,** New Orleans, La.: **Injuries of the Abdomen—Preventive and Prophylactic Aspects.**—The destructive and complicated character of abdominal wounds incurred in modern warfare, and the difficulty of quickly transporting these casualty cases, is responsible for an appallingly high mortality rate, and is forcing the consideration of abdominal injuries from the preventive and prophylactic standpoints. Fortunately, not only are there methods whereby the present number of immediately fatal injuries can be reduced, but there are also means whereby more of the less seriously injured abdominal casualty cases may be saved. Preventive measures for the reduction of the total number of injuries include education in respect to precautions that should be taken by armed forces and civilians at times when the danger of incurring abdominal injuries can be reasonably anticipated, the provision of adequate shelters for protection in case of airplane or artillery raids, armor protection for vehicles and equipment, and the adoption of some type of body armor. The author discussed various types of materials which have been employed for

body armor, and showed slides illustrating body armor which has already been devised as well as a suggested modification, or new type of body armor, designed to afford maximum protection with minimum increased weight. Of the prophylactic measures for the reduction of the serious consequences and complications of abdominal injuries, some may be instituted beforehand, while others are applicable after injury is incurred. Measures which may be employed before injury is incurred are concerned with reducing the incidence of severity of peritonitis resulting from perforation of the hollow alimentary tract viscera. In this connection the author discussed the possibility of administering sulfanilylguanidine for the purpose of accomplishing relative sterilization of the gastrointestinal contents, as well as transforming the intestinal flora by means of preliminary administration of cultures of lactobacillus. Measures which may be employed after injury is incurred are concerned with avoidance of delays in transportation, the use of motorized mobile hospital units, the application of improved methods for the treatment of peritonitis and wound infection, and the employment of new methods for the study and treatment of shock and hemorrhage. A mobile shock cart, which consisted of a compact arrangement of the apparatus and materials used in the modern study and treatment of shock and hemorrhage, was illustrated.

14. **Owsley Grant,** Louisville, Ky.: **The Use of Air Pyelogram in Diagnosis.**—The use of gas or air as a medium in pyelography is not new. Difficulties following the use of air have been due to disregard of the fundamental principles of the method. Air embolism can be wholly obviated. Following a description of the method, the author reviewed the contraindications, which consisted essentially of: (a) conditions under which retrograde pyelography would be inadvisable and (b) frank renal hematuria. The air method is of inestimable value in accurately and positively locating the position of small stones or fragments of large stones. There have been no untoward effects in the author's experience, and postoperative reactions have been less than when other media have been employed.

15. **J. Garland Sherrill,** Louisville, Ky.: **The Management of Bilateral Renal Stones.**—The author presented a historical résumé concerning stones of the urinary tract. It is frequently difficult to decide upon the best method of managing bilateral stone cases. Some writers advise operating upon the side of the least damaged kidney first, while a contrary procedure is advocated by others. Complications are more common in bilateral calculus cases. The efficiency with which the remaining kidney takes on the function of the one which has been removed was discussed. Patients who have had bilateral stones must be advised to live in a manner which minimizes any deviation from the normal.

In discussing the last two papers, **Thomas S. Cullen,** Baltimore, cited some personal experiences as a sufferer from stones. **Henry D. Furniss,** New York City, spoke favorably of air pyelography, especially when it is desired to do a pyelogram with a patient in the erect position. He believes that carbon dioxide is safer than air. **Irvin Abell,** Louisville, Ky., stated that so far no studies made have elucidated the formation of renal calculi, and for this reason a rational method of treatment has not yet been evolved. Abell cited that calculi are unilateral in 75 per cent of cases and bilateral in 25 per cent of cases. In bilateral cases the stones may be of equal size, or the stone on one side may be much larger than the one on the other side. He favors removing first the stone on the side showing the greatest function. When large calculi are present on both sides, it may be better to avoid any surgical intervention. **Lawrence R. Wharton,** Baltimore, believes that operation should be done if possible, even when large stones are present on both sides. He emphasized conservatism in respect to performing nephrectomy.

16. **William Perrin Nicolson, Jr.,** Atlanta, Ga.: **Tuberculosis of the Breast.**—Tuberculosis of the breast is more common than is generally supposed. Unnecessary radical operations may be averted by early recognition of this lesion. The present report is based on seven cases. The history of the surgery of tuberculosis of the breast through 1939 was reviewed. There have been 500 cases in the literature. The suggested routes or mechanisms whereby the infection becomes established are as follows: (a) via the duct, (b) through skin or nipple abrasion, (c) through the blood stream, (d) through the lymphatics, and (e) by contiguity of tissue. There was a history of trauma in 7 per cent of the cases. Tuberculosis of the breast is more common during the childbearing age. Early diagnosis from carcinoma is difficult. Differential diagnosis must be made from carcinoma, sarcoma, benign fibroepithelial tumors, chronic cystic mastitis, gumma, plasma cell mastitis, fat necrosis, and pyogenic mastitis. The average age was 36.4 years, with a range of from 16 to 70 years. The average duration of symptoms was 13.6 weeks. The author advocated simple mastectomy as the operation of choice. Only fourteen cases of bilateral tuberculosis of the breast have been reported. The author's case occurred in a 17-year-old girl.

Discussion: **John L. McGehee,** Memphis, Tenn., reported five cases in addition to those which had been reported up to 1934. These five cases occurred among 932 breast cases at the John Gaston Hospital. McGehee felt that biopsy was necessary in order to confirm clinical impressions in such cases. **Julian Moore,** Ashville, N. C., inquired in regard to the existence of tuberculosis in other areas in the cases reported by Nicolson. **Willard H. Parsons,** Vicksburg, Miss., reported the case of a patient with tuberculosis of the breast from whom three years previously he had removed a kidney for tuberculosis. A simple mastectomy was done and now, eight years afterwards, there has been no recurrence. **Arthur M. Shipley,** Baltimore, reiterated the possibility of confusing tuberculosis of the breast with carcinoma of the breast. He felt that in only a few instances is there evidence of tuberculosis elsewhere.

17. **Frank H. Lahey,** Boston: **Aids in Avoiding Serious Complications in Thyroidectomy.**—In a series of 19,700 thyroid cases at the Lahey Clinic, there has been a mortality of 0.76 per cent. There has been an incidence of 0.3 per cent of recurrent laryngeal nerve injury in the last 5,000 cases. There have been 10 cases of tetany in the entire series, and none in the last 4,000 cases. Lahey felt that it is important that the surgeon rather than the internist should study and prepare thyroid cases before operation. He stressed the importance of recording one's impressions when the patient is first seen in regard to the number of stages of operation which probably will be needed. Unless this is done, the improvement which results from preoperative preparation may lead to the undertaking of undesirably extensive operations. The age of the patient, the gain or loss of weight, and the duration of the disease must be taken into consideration in estimating thyroid cases. The administration of 10 per cent glucose just before operation was advocated in order to reduce the number of postoperative thyroid reactions. Lahey felt that the pulse pressure is the best single indication of toxicity. An increase or widening of the pulse pressure during operation indicates an increasing toxicity and serves to indicate that operation should be stopped. The use of local anesthesia was deprecated and, although cyclopropane was considered to be the best anesthetic, the dangers associated with the use of this substance were reviewed. Lahey has personal knowledge of three cases in which ventricular fibrillation and death followed the administration of cyclopropane, and for this reason he advocated the administra-

tion of this gas at a low concentration. As a means of observing heart function during operation, a visible electrocardiogram projected onto the wall of the operating room is now being employed in his clinic. Intratracheal anesthesia was advocated for use in many cases, and the desirability of performing tracheotomy early in cases in which there is any duskiness was stressed. Variations in the course of the recurrent laryngeal nerves were described, and exposure of the nerves during operation was advocated, as a means not only of protecting the nerves, but also of safely permitting the removal of sufficient thyroid tissue, to prevent so-called recurrence or continuance of symptoms. Inadequate exposure of the gland was considered to be a frequent cause of postoperative hemorrhage. Transverse division of the strap muscles was advocated as a routine procedure. The author illustrated cases in which poor skin scars followed thyroidectomy, and he discussed means of avoiding such disfiguring scars.

18. **Warren H. Cole,** Chicago, Ill.: **Precautions in the Surgical Treatment of Thyrotoxicosis.**—Since neurocirculatory asthenia, tuberculosis, and endocarditis may be confused with thyrotoxicosis, these conditions must be considered in differential diagnosis. Cole believes that ambulatory preparation of the thyrotoxic patient is desirable unless cardiac decompensation exists or unless the patient is severely toxic. It is important to recognize and to treat adequately associated diseases, such as diabetes. Mortality may be favorably influenced by employing multiple-stage operations in certain cases. The following were presented as criteria for operability: (a) gain in weight, (b) lowering of resting pulse rate to 115, (c) lowering of the basal metabolic rate to 50, (d) improvement in symptoms. Local anesthesia was deprecated and the author expressed a preferance for ethylene. Allowing the patient to wait for a long time in the operating room before operation is started produces a very unfavorable psychic effect. It is usually unsafe for the surgeon to change his mind during the course of operation in regard to the extent of operative procedure. Glucose solution should be administered intravenously before and after operation. Cole gives Lugol's solution for as long as three weeks postoperatively. Tracheotomy should be done immediately when stridor indicates hemorrhage or nerve injury. Postoperative oxygen therapy is effective in preventing or treating thyroid crises.

Discussion: In considering the mechanism whereby ligature of one or both superior thyroid arteries produces a good effect, **George Curtis,** Columbus, Ohio, believes that improvement is not due entirely to reducing the blood supply, but that at least part of the benefit from this procedure is due to interruption of nerve conduction. There is a negative calcium balance in hyperthyroidism, and for this reason Curtis some time ago began administering calcium preoperatively along with large amounts of vitamin D, and he feels that calcium therapy has prevented severe postoperative storms in his cases. Thyroidectomy arrests the negative calcium balance. **Robert Dinsmore,** Cleveland, Ohio, pointed out that lowering of the pulse rate is an important index of the thyrotoxic patient's improvement. In discussing the matter of the exposure of the recurrent laryngeal nerve in the course of thyroidectomy, he observed that Lahey does not expose the entire nerve. Dinsmore expressed the belief that postoperative psychoses are not due to the hyperthyroidism or the operation for hyperthyroidism. **Robert Bartlett,** St. Louis, gave a brief report on a fifteen-year study of goiter cases which had been under the care of himself and his associates in private practice. In the period between 1926 and 1930, the mortality was 3.1 per cent; whereas, in the period between 1931 and 1940 the mortality was 1.7 per cent. He and his associates have not done upper

pole ligations since 1931. Since 1935 there have been no deaths in crisis, and no severe reactions have been observed. **Harold Foss,** Danville, Pa., is convinced that there are various ways of obtaining equally good results in the management of hyperthyroid patients. When the mortality is high, it indicates to him that more multistage operations should be done.

In closing the discussion, Lahey advised against operating on borderline or doubtful cases. He felt that patients in such cases should be allowed to go away on a trip and that they be reassessed following their return. This, he felt, will eliminate unnecessary operations. A low basal metabolic rate does not indicate safety, although a high basal metabolic rate does indicate toxicity. He felt that at least some of the benefits accruing from preliminary pole ligation were due to the conditioning of the patient to operative procedure.

20. **Loyal Davis,** Chicago, Ill.: **Endocrine Studies in Patients With Subtotal Hypophysectomy.**—Davis observed that, although visual disturbances may be relieved by hypophysectomy, some of the patients continue to have endocrine disturbances postoperatively. He reviewed methods for maintaining or restoring the pituitary or master gland influence on the target glands; i.e., the thyroid, the adrenals, and the gonads. Hypophysectomy causes a lowering of basal metabolic rate and a rise in cholesterol. Studies conducted in conjunction with the present work also included estimation of adrenal cortex activity by the Wilder test, carbohydrate balance, gonadotropic function, and parathyroid function. These studies were carried out in 25 cases, 18 of which were hypopituitary and 7 of which were acromegaliac.

Discussion: **Waltman Walters,** Rochester, Minn., considered such studies as Davis had made as important in furnishing data concerning the role of the pituitary and other ductless glands, and in permitting interpretation of the confusing implications of such conditions as hypoglycemia not due to adenoma of the islands of Langerhans. **Emil Novak,** Baltimore, discussed Frölich's syndrome in relation to its gynecologic aspect. Novak spoke of the unsatisfactory status of substitution therapy due to the unknown chemical nature of the pituitary product. **Ambrose H. Storck,** New Orleans, La., noted that, because estrogenic hormones inhibit the production of thyrotropic pituitary hormones, diethylstilbestrol or other estrogenic substances have been given to a small number of hyperthyroid patients who could not be brought into good condition by means of rest, calcium, iodine, a high caloric diet, and vitamins. The number of cases in which apparently beneficial effects following this type of therapy have been observed is still small, but the results so far have been at least encouraging.

21. **J. Barrett Brown,** St. Louis, Mo.: **Reconstruction of Cleft Lips.**—This presentation consisted principally of motion pictures accompanied by comments by the author. Brown emphasized the importance of always letting some member of the family see a cleft lip patient before operation is undertaken. In discussing the influence of heredity in the development of cleft lip, it was observed that children of parents who have had cleft lip do not necessarily have cleft lip. Nasal correction should always be done in conjunction with the lip repair.

Discussion: **H. L. D. Kirkham,** Houston, Tex., pointed out that standard procedure in the repair of cleft lip is oftentimes impossible because of the many different problems which may be present in individual cases. In the instance of double defects Kirkham repairs one defect at a time. If a tight upper lip follows a repair, he transplants a piece of the lower lip into the upper lip.

22. **Howard M. Clute,** Boston, Mass.: **Jejunostomy for Postoperative Feeding.**—Jejunostomy for postoperative feeding was presented as a procedure which may be lifesaving. Reference was made to the relative malnutrition which is common in the general population. In stomach cases malnutrition is particularly likely to be pronounced. It is important to realize that subclinical manifestations or states of subnutrition exist, and may be responsible for postoperative hypoproteinemia. Complementary jejunostomy, performed at the time of principal operation, has been employed by the author in over fifteen cases in which there were lesions of the stomach and biliary tract. There were no deaths in this series of cases. A mixture of skimmed milk, thiamin, egg, vitamin C, and haliver oil with viosterol is administered through the tube postoperatively in amounts from 1,500 to 2,000 c.c. daily. Jejunostomy is usually performed in a loop of bowel 20 to 30 cm. below the ligament of Treitz. The first purse-string suture surrounding the jejunostomy tube is anchored to the tube, and a second purse-string suture anchors omentum to the area of the ostomy. When no omentum is present, the ostomy site is brought to the peritoneum of the wound edge. The ostomy openings have closed within from two to three days following removal of the tube, and there has not been a complicating factor in any case.

Discussion: **Shelton Horsley,** Richmond, Va., stated that he has employed the method described by Clute, but that he prefers a mushroom catheter to a whistle-tip catheter. He subsequently cuts off the tube and allows the mushroom tip to be passed per rectum. Horsley referred to the undesirable effect produced by indwelling gastroduodenal catheters, and for this reason he does gastrostomy in many gastric resection cases. He uses a sharp hemostat instead of a scalpel for making the opening into the stomach, because this procedure produces a gridiron effect and prevents leakage when the tube is removed.

23. **Harold L. Foss,** Danville, Pa., **Secondary Operations on the Gall Bladder and Biliary Ducts.**—After commenting on the frequency of biliary tract disease, Foss presented observations based on 2,485 biliary tract patients in whom 140 secondary operations were performed. The average age of the patient at the time of the first operation was 40 years, and the average age at the time of the second operation was 48 years. Ninety-five of the secondary operations followed cholecystostomy, the secondary operation in most cases consisting of cholecystectomy. Thirty-three patients upon whom secondary operation was performed had had cholecystectomy and 11 of these had had a common duct stone. Six of the secondary operations revealed biliary duct stenosis. There were stones in the gall bladder or ducts in 58 per cent of the secondarily operated cases. Fifteen per cent of the cases had dilated ducts. Eleven of the cases had been operated upon two or more times before Foss saw them. In 7 of the 140 patients upon whom secondary operations were performed, nothing but exploration was done. The hospital mortality on the entire series of 140 cases was 8.5 per cent. Routine exploration of the dilated common duct was advocated. It was not considered that x-ray examination of the ducts in the operating room is practical. Foss observed that it is surprising how often the findings at the second operation are not in keeping with the symptoms and signs presented preoperatively. Cholecystectomy performed for noncalculous gall bladder disease is frequently followed by unsatisfactory results. The use of cotton for ligature and suture material was lauded and was advocated as a means of reducing the frequency of postoperative hernia and wound infection. (N. B. This paper was discussed in conjunction with the papers of Newell and Edwards, to follow.)

25. **A. P. Jones,** Roanoke, Va.: **A Method of Handling the Appendical Stump.**—The author reviewed the methods of treating the appendical stump which have been advocated. The blind sac produced by ligation of the base of the appendix and invagination of the stump by means of purse-string suture may become the site of an abscess which may subsequently rupture into the peritoneal cavity. Inversion of the appendix without its ligation was considered to be dangerous on account of the possibility of peritoneal contamination. It was not considered that simple ligation of the appendix is a satisfactory procedure. The author described the method which he employs, which consists of turning back a cuff of peritoneum in the region of the base of the appendix, placing a double loop of catgut about the appendix, holding the loops of catgut close to the appendix by means of hemostat, introducing a purse-string suture, and then cutting the loops of catgut close to the point where they are grasped by hemostats, and inverting the stump by means of the hemostats still attached to the remaining short loops surrounding the base of the appendix. He has employed this method in 126 cases with no mortality. Fifty of the cases had acute appendicitis.

Discussion: **Shelton Horsley,** Richmond, Va., contended that the simple ligation method is quick, simple, and adequate. In 1,142 cases in which this method has been employed, there have been 8 deaths, or a mortality of 0.7 per cent.

26. **E. Dunbar Newell,** Chattanooga, Tenn.: **Report of a Case of Rupture of the Common Duct.**—Spontaneous rupture of the common bile duct is very rare and few examples of this lesion, in which there was not associated trauma, operation, or an impacted stone, have been reported in the literature. The author was able to find only two other similar cases reported. The patient on whom the present report is based was a diabetic who had had epigastric distress for eight years. There was no jaundice. A preoperative diagnosis of ruptured peptic ulcer was made. At operation, exploration revealed a dilated common duct and there was effusion of bile under the peritoneum overlying the bile duct. Several small cholesterol stones and some "mud" were found in the duct. The gall bladder was removed and the common bile duct was drained for twelve days postoperatively. A follow-up one year later revealed the patient to be in excellent condition, having gained fifteen pounds. It was believed that the rupture occurred at an inflamed weak spot or that it might have been due to an impacted stone in the wall. Some details of the two other cases reported in the literature were presented.

27. **C. R. Edwards,** Baltimore, Md.: **Acute Cholecystitis With Perforation Into the Free Abdominal Cavity.**—The present report is based on twenty-one cases of acute cholecystitis which were admitted to two hospitals in Baltimore. There was an 11 per cent incidence of perforation. Only 75 per cent of the acute cases were operated upon, the rest of the perforations being found at autopsy. The history and physical signs were typical in all cases. The author does not believe that x-ray examination is important in the diagnosis of this condition. Partial resection or cholecystostomy was done in most of the cases upon whom operation was performed, but the author believes that cholecystectomy should be done if possible.

Discussion: **Thomas S. Cullen,** Baltimore, discussed Edwards' paper and presented observations in regard to rupture of the gall bladder, especially in respect to stones which became encapsulated after extrusion into the peritoneal cavity. **Charles Gordon Heyd,** New York City, in discussing Foss' paper referred to his own observations based on a review of 4,000 cases with biliary tract disease. Forty-two of the

cases required exploration of the common duct at the second operation (thirty-six of these patients had their first operation elsewhere), and in the majority of these cases calculi were found in the duct. Heyd expressed his strong conviction that cases of acute cholecystitis should be operated upon, as in most instances the rupture is associated with acute peritonitis and in only a comparatively few cases does local abscess formation occur. Before operating for acute cholecystitis, six to twenty-four hours of preparation should usually be allowed because in a group of cases operated upon immediately there was a 24 per cent mortality; whereas, the mortality is much less when preliminary preparation is done. **Robert L. Rhodes**, Augusta, Ga., considered that blood chemistry studies, which reveal low chloride or high uric acid levels, indicate the need for preoperative preparation in biliary tract cases. The liver should be given preeminent consideration. General hygienic care is important and will oftentimes relieve the distressing symptoms which persist in some instances following biliary tract operations. **Howard Clute**, Boston, in discussing Foss' paper, described a vitallium tube which has been devised for use in reconstruction operations on the common duct. Clute reported a recent successful bile duct operation on a patient who had been previously operated upon four times. **George Bunch**, Columbia, S. C., reported two cases in which there was an acute exacerbation of gall bladder disease during the course of treatment for fracture of the femur. In one of these cases the gall bladder ruptured, in the other case the gall bladder was found to be full of stones, but there had been no rupture of the gall bladder wall. **Frank Lahey**, Boston, briefly reviewed two cases in which a rubber tube was used to span defects or loss of substance of bile ducts. One of these cases was operated upon four years ago, while the other was operated upon two years ago. At present, both are well. Lahey cautioned against allowing a tube introduced into the common duct to extend into the duodenum. The tube should be of a size larger than the sphincter of Oddi. Exploration of the common bile duct is especially indicated in the presence of acute cholecystitis, in which there is frequently infected bile and stones in the duct.

28. **Warfield M. Firor**, Baltimore: **The Use of Sulfanilylguanidine in Surgical Patients.**—Observations and experiences based on 12 surgical patients who rereceived sulfanilylguanidine before operation on the colon were presented. Although the author did not feel justified in formulating definite or final conclusions at present, it was considered that at least 2 of the cases would have died if the concentration of coliform bacteria had not been reduced before operation. The author also felt that the intestinal wounds in 3 cases would have failed to heal per primum without the drug. In 2 cases open anastomosis was successfully performed without the slightest evidence of subsequent infection. Firor referred to the observation of Marshall and his co-workers that this drug, when given orally, is less toxic than sulfapyridine or sulphathyzol. Sulfanilylguanidine is poorly absorbed from the intestinal tract, and the concentration of coliform bacteria in the feces of mice is greatly reduced after the oral administration of the drug. Furthermore, these workers found that the new compound is as active as sulfapyridine against pneumococcus infection in mice, and on the basis of in vitro studies they showed that it is as effective as is sulfanilamide against several other pathogenic bacteria.

Discussion: **Leo Brady**, Baltimore, stated that, through the courtesy of Firor, he and his associates have had the opportunity of using sulfanilylguanidine in 2 cases, in both of which it was considered that the administration of the drug prevented the development of peritonitis. Brady commented on the absence of nausea and vomiting, and found that the patients were willing to take the drug almost as soon as they reacted from the anesthetic. **Harvey B. Stone**, Baltimore, has employed

this drug in 6 cases, in all of which there was infection of the colon of one kind or another. All of the cases survived operation. He felt, however, that much additional experimental work must be done in order to evaluate fully the drug. The solubility of the drug in water, the lessened absorbability from the alimentary tract, and the specificity for the colon group obviously make sulfanilylguanidine an agent almost ideally designed for attack upon the bacterial flora of the large bowel. Apparently, the high degree of effectiveness is attained at the end of six or seven days of administration. Several days after the drug is discontinued, bacteria rapidly reappear. Therefore, it seems wise to give it for six or seven days prior to the planned operation and to continue the administration of the drug six or seven days after operation. **Arthur M. Shipley,** Baltimore, reported a case in which sulfanilylguanidine was administered preceding resection of the right colon and anastomosis between the terminal ileum and the transverse colon. There was an amazing drop in the bacterial count during the preoperative preparation period and there was no evidence of infection in the wound. **Frank H. Lahey,** Boston, asked if there have been any contraindications or any evidences of toxicity in the use of the drug.

In closing, Firor stated that, with reference to the degree of absorption, it has been found that the blood level concentration ordinarily runs between 2 and 4 mg. per cent, and in only two instances did it go over 5 mg. per cent. The dosage was experimented with in this group of patients, and at present it is felt that 50 mg. per kilogram of body weight every eight hours for a week before operation and a week after operation is perfectly safe. It has been found in some experimental work that far better results are obtained by giving the drug at eight-hour intervals than more frequently or in a single dose. Evidence of toxicity or contraindications to the use of the drug have not been found. Marshall has been employing the drug in cases of bacillary dysentery, with astounding results when it is given in the first three days of illness. He added that a report on this use of the drug would appear in the January issue of the *Bulletin of the Johns Hopkins Hospital.*

29. **Frank S. Johns,** Richmond, Va.: **Recurrent Carcinoma of the Rectum.** Johns reported the case of a male patient who had a "recurrence" of carcinoma in the region of the stoma, which followed a Kraske operation performed fifteen years previously for a grade II carcinoma. Examination of the specimen, removed by combined abdominal and posterior resection at the second operation, revealed the carcinoma to be of grade III, but the pathologist reported "a striking resemblance in the cell morphology to the previous growth" and that "it was probably of similar cell origin." A year and a day have now passed since the second operation and on recent examination the patient, now 42 years old, seems to be in good health.

30. **Frederick A. Coller,** Ann Arbor, Mich.: **Regional Lymphatic Metastasis of Carcinoma of Colon.**—Coller presented the results of observations made on clarified specimens of colon and attached mesentery in respect to the occurrence and distribution of metastases. By this method, employed by associates of his, a much higher percentage of nodes was demonstrable. It has been possible to demonstrate fifty-two lymph areas per specimen instead of an average of fourteen by older methods. In 46 cases there were 28 with metastases, an incidence of 60.87 per cent. By means of charts of various parts of the colon, areas and directions of metastatic spread were indicated. Frequently, no correlation is found between the size of the colon tumor and the presence or extent of metastases. Likewise, in his series there was no correlation between the duration of the disease and the degree of metastasis.

Metastases, however, do parallel the increasing grade of malignancy of the tumor. Many metastatic nodes are not palpable, and the size of lymph nodes is no index of metastasis. Therefore, operative procedures must be based on anatomical knowledge rather than on detectable lymph nodes.

31. **Henry W. Cave**, New York City: **Mortality Factors in the Surgical Treatment of Ulcerative Colitis.**—The author has done 90 operations on 50 individuals, with a mortality rate of 22 per cent. In 1939, 59 people in New York City died of ulcerative colitis. The horror of having a terminal ileostomy causes disastrous delays in many cases. Hemorrhage and peritonitis are the direct causes of death. Recently, sulfanilamide, administered orally, has been employed in the management of these cases. Ulcerative colitis is a cyclic recurring disease, and it is often difficult to choose the proper time for surgical intervention. In selecting cases for operation, judgment is based on a consideration of whether or not the disease is undergoing uninterrupted progression, or whether there are remissions, either one of which circumstances constitutes indication for surgical intervention. Operation should be done during a period of quiescence. Preoperative medical observation and preparation are very important.

Discussion: **Frank Lahey**, Boston, stated that at the Lahey Clinic there have been 280 cases of ulcerative colitis, with 80 complete colectomies and 3 deaths. There were 14 colectomies with no deaths. There have been 5 restored ileostomy cases. In emergency or extremely ill cases only a loop type of ileostomy is performed; whereas, in elective cases an end type ileostomy is done. Lahey felt that any individual who has had two episodes of colitis should have an ileostomy. Lahey felt that not every case with a rigid colon is a candidate for colectomy. In order to avert pulling of the intestine into the abdomen, he advocated fixation of the mesentery to the peritoneum.

Discussion: **Harvey B. Stone**, Baltimore, noted that sulfanilylguanidine has been tried in a few cases of ulcerative colitis, and it is believed that the drug is of no value in the treatment of the basic lesion. However, it is considered to be of value in preoperative preparation in order to reduce the number of the colon group organisms. Stone also emphasized the importance of early ileostomy.

32. **Harvey B. Stone**, Baltimore: **Results With the Fascia Plastic Operation for Anal Sphincter Repair.**—The present report is based on 30 operations performed by various surgeons in Baltimore. The author reviewed the operative procedure which he has previously described. The operation may be employed to advantage in certain cases of anal fistula, in congenital abnormalities, following operation for hemorrhoids in which there has been loss of sphincter function, following rectal cancer operations, in certain cases of perineal lacerations, prolapse of the rectum, and congenital megarectum, following trauma, and in some cases of anal ulcer. The results have been excellent in 12 cases (40 per cent), good in 9 cases (30 per cent), fair in 5 cases (16.6 per cent), and unsatisfactory in 4 cases (13.3 per cent). When the gluteal muscles are also impaired, as in certain cases of spina bifida, the operation is of no value. The author emphasized the importance of a period of training in order that the individual might gain full benefit from this operation. Since it is necessary to train the patient to contract the gluteal muscles, it is unreasonable to expect good results in very young children, or in adults with low mentality. The procedure, in case of a primary failure, may be repeated.

Discussion: **Harry Warthen,** Richmond, Va., presented the case of a child in which the procedure described by Stone had been employed. The results were very satisfactory. **Deryl Hart,** Durham, N. C., reported a case of a patient with congenital incontinence of feces in which strips of fascia were employed to bridge the ends of a deformed sector of the anal sphincter.

33. **W. L. Estes, Jr.,** Bethlehem, Pa.: **End Results in the Treatment of Inguinal Hernia by a Fascia-to-Fascia Rectus Sheath Closure.**—The factors which influence the recurrence of hernias include the age of the patient, the type of the hernia, the character of the patient's tissue, and the type of operation. After discussing various types of operations for hernia, the author described in detail the procedure which he employs. Following high ligation of the sac and closure of any defect in the transversalis fascia, a flap of rectus abdominis muscle sheath is raised and then sutured to Poupart's ligament. The line of suture should not be continued above the normal level of the internal inguinal ring, as such a procedure will cause pressure on the cord and testicular atrophy will result. The outer flap of the external oblique fascia is sutured to the medial edge of the defect produced in the rectus abdominis muscle sheath. The procedure has been employed in 394 cases, 86 per cent of which have been followed up. All but 16 of the cases followed up were seen and examined. There were 4 recurrences within a year following operation. In 317 indirect hernias there was a recurrence of 0.4 per cent. In 80 direct hernias there was a recurrence of 2.77 per cent; and in 19 recurrent hernias there was a recurrence of 12.5 per cent. In a total of 416 operations there was a postoperative recurrence in 5, or an average of 1.2 per cent.

34. **Charles R. Robins,** Richmond, Va.: **Why Inguinal Hernia Recurs.**—The anatomical features, and methods of diagnosing hernias were reviewed. Direct and indirect hernias are frequently present in combination. Most recurrences occur within one year. The shutter action of the flat muscles of the abdominal wall was discussed, as was also the thick ligamentous fascia which runs along the top of the pubic bone. The author advocated the use of fascial sutures.

Discussion: **Bradley Coley,** New York City, felt that the many methods advocated for the repair of hernia evidence the imperfect results frequently observed following operations for hernia. He advocated the use of nonabsorbable suture material, particularly silk, which averts wound infection and rupture. Operations which involve taking a bite in muscles in the region of the internal ring interfere with the shutter action of the muscles in that region. Many slight direct bulges may best be left alone. **Harold Foss,** Danville, Pa., felt that simple types of operations are generally best. He prefers silk or cotton to fascia. In addition to the use of nonabsorbable suture material, Foss considered that adequate obliteration of the inguinal canal was important in effecting a cure in hernia. **Willard Bartlett,** St. Louis, discussed the occurrence of atrophy of the testicles following hernioplasty. Because of the possibility of bilateral atrophy following operation, the advisability of operating upon but one side at a time should be considered. **G. B. Rhodes,** New York City, described an operation in which a triangular flap of rectus sheath is employed. The flap is passed through a slit in the external oblique fascia and then sutured to Poupart's ligament. **Frederic Bancroft,** New York City, has employed an operative procedure which represents a modification of the type of operation performed by Estes. Believing that the bladder, when the patient is in the erect position, plays an important part in the recurrence of hernia, he advocated exposing the bladder and drawing it medially by means of sutures

through the bladder and through the rectus abdominis muscle sheath. **Donald Guthrie**, Sayre, Pa., voiced his favorable experience with the use of cotton as suture material.

35. **J. Shelton Horsley,** Richmond, Va.: **Resection of the Duodenum for Tumor of the Ampulla of Vater.**—Techniques which have been developed for the excision of the second portion of the duodenum and the head of the pancreas were reviewed. Horsley stated that the Whipple procedure has been modified so that the common duct is anastomosed end-to-side to a loop of jejunum, and that a jejunojejunostomy is performed in addition to the performance of a gastrojejunostomy and excision of the duodenum and pancreas. A case was reported in which Horsley resected part of the second portion of the duodenum along with a portion of the pancreas on account of a tumor located in the region of the ampulla of Vater. The tumor was a fibroadenoma. Although wound healing, as revealed at autopsy, was quite satisfactory, the patient died of uremia.

36. **R. Arnold Griswold,** Louisville, Ky.: **Perforated Peptic Ulcer.**—This report is based on 111 cases. There was a ratio in this series of white to colored patients of 4:3. Only 65 per cent of the patients vomited after perforation had occurred. Only 3 were in shock, as indicated by a blood pressure determination, although a clinical appearance suggesting shock was present in other cases, and the author drew attention to the fact that pallor may be misleading in suggesting the existence of shock in ruptured ulcer cases. Seventy-three per cent of x-rays revealed air beneath the diaphragm. All patients who were distended at the time of operation died. Nine of the 111 patients were not operated upon because they were first seen long after perforation. The author has discontinued the use of spinal anesthesia because of 2 deaths which followed its administration. He prefers a transverse abdominal incision and he advocated simple closure of the perforation with two rows of sutures. Sulfanilamide is instilled into the peritoneum and into the wound in some cases. Ordinarily, no intraperitoneal drainage is attempted. Silk sutures are employed for closure of the wound in the abdominal wall. It was considered that the presence of streptococci in the peritoneal cavity influences the mortality following perforated peptic ulcer.

Discussion: **Ambrose H. Storck,** New Orleans, La., presented some of the findings in a study recently completed at Tulane University by Ochsner and DeBakey, based on a review of approximately 23,000 cases of perforated peptic ulcer, as well as some findings revealed from a review of records at the Charity Hospital at New Orleans. The incidence of perforation in peptic ulcer in the cases collected from the literature was 13.2 per cent; whereas, in the Charity Hospital cases it was 8.09 per cent. There has been an increase in recent years in the percentage of perforation of peptic ulcers in the Charity Hospital series. Whereas perforating duodenal ulcer occurs most frequently in the ages between 20 and 40 years, the peak incidence of perforation of gastric ulcer is in individuals about 50 years old. In 11,305 cases in which the location of the perforation was accurately recorded, 51.2 per cent were duodenal, 38.9 per cent were gastric, and 9.8 per cent were "pyloric." There was a constant direct relationship between the death rate and the age of the patient, and the mortality increased progressively in relation to the number of hours elapsed between the time of perforation and the time of operation. Although the mortality was highest in the group of cases in which local anesthesia was employed, this type of anesthesia was frequently employed in cases of long duration or in poor risk patients. The relatively low mortality when spinal anesthesia was administered suggests that this type of anesthesia is preferable to general anesthesia. The mortality following various operations was as follows: simple closure, 25.9 per

cent; closure plus gastroenterostomy, 20.4 per cent; excision plus closure or pyloroplasty, 15.9 per cent; gastrectomy, 13.5 per cent. The relatively high mortality following simple closure no doubt was due to the employment of this procedure in the majority of patients who were in poor condition. The very low mortality following gastrectomy reflects the skill and experience of the relatively few surgeons who employed this procedure. Not only is excision of the ulcer plus closure or pyloroplasty effective as a means of meeting the problem of perforation, but the follow-up results after this type of procedure are very satisfactory. Relatively poor results following simple closure might be averted if more of the patients on whom this procedure is employed were properly instructed in regard to postoperative, dietary, and general hygienic regimen. In 942 cases in which the cause of death was definitely stated, peritonitis was found in 57.1 per cent, pulmonary lesions were present in 20.7 per cent, and other causes were reported in 22.1 per cent. **Robert Rhodes,** Augusta, Ga., reported a case of duodenal ulcer in which there was no air bubble demonstrable by x-ray. Following simple closure of the perforation, this patient subsequently had two perforations at points distal to the site of the first perforation. **Albert Singleton,** Galveston, Tex., discussed the occurrence of perforation of peptic ulcers in infants. Recently, Singleton operated upon a 14-hour-old infant, and he has operated upon another infant 3 days old. There are many cases of early perforation of peptic ulcer recorded in the literature, including one case in which perforation occurred in utero. **John M. T. Finney, Jr.,** Baltimore, illustrated a familial tendency or predisposition to ulcer, stating that he had operated upon three brothers for perforated ulcer. Two of these patients gave no ulcer history. All of them lived. Finney referred to the use of the round ligament of the liver as a plug in cases in which simple closure is done. **Joseph Donald,** Birmingham, Ala., stated that excision of the ulcer followed by pyloroplasty has been used at the Hillman Hospital for the past several years with very gratifying results. He believes that the use of the transverse abdominal incision reduces the incidence of wound disruption.

In closing, Griswold referred to the employment of the Gatch procedure of folding nonindurated stomach and duodenal tissue over the site of perforation.

37. **George Curtis,** Columbus, Ohio: **Mediastinal Ganglioneuroma.**—Ganglioneuromas may occur throughout the body, but they are mainly found along the course of sympathetic nerve trunks. Most frequent sites are in the neck, thorax, abdomen, and pelvis. The author also discussed the closely related tumors of the adrenal gland. Mediastinal ganglioneuromas are uncommon, but the frequency with which they are recognized is increasing because of more x-ray examinations, and advances in thoracic surgery which permit exploration as well as removal of these tumors. The case upon which the author's present report was based was that of a 35-year-old nurse. The tumor was successfully removed by thoracotomy. Preoperative recognition of the presence of the tumor was the result of routine x-ray examination of the chest, as there were no symptoms. Preceding the removal of the tumor, preparatory pneumothorax was done. Gross examination of the specimen revealed myxomatous areas, fibrillar areas, and hemorrhagic areas. Microscopic examination revealed it to be a ganglioneuroma. Of the 200 ganglioneuromas so far reported in the literature, about 30 have been mediastinal.

Discussion: **Julian Moore,** Asheville, N. C., spoke of extrapulmonary intrathoracic tumors. He deplored the fact that many patients with such tumors are not given the benefits which may be afforded by modern chest surgery. All these tumors were considered by him to be potentially malignant. Diagnostic procedures include pneumothorax, bronchoscopy, and therapeutic tests by means of x-rays. In advocating cyclopropane or ether as an anesthetic, Moore remarked that, although positive pres-

sure anesthesia is necessary, he does not believe that intratracheal anesthesia is necessary. In order to guard against infection and emphysema, he believes that a catheter should be inserted and suction applied postoperatively.

38. **G. V. Brindley,** Temple, Tex.: **Carcinoma of the Fundus of the Uterus.**—This report is based on 92 cases. The ratio of uterine carcinoma to uterine sarcoma is 6:1. Eighty per cent of the patients were past 50 years of age. Abnormal bleeding is the most common symptom. Carefully performed curettage is the only accurate diagnostic method. All fibroids should be carefully examined immediately following their removal because some will be found to have areas of carcinoma in the fundus of the uterus. The highest percentage of cures in carcinoma of the fundus of the uterus is obtained by means of hysterectomy supplemented with radium or x-ray. The hospital mortality in the present series was 1.1 per cent. The degree of malignancy is low in two-thirds of the cases, and 79 per cent remained cured five years or longer by means of surgery and irradiation. Only about 40 per cent of five-year cures follow irradiation alone. The low-grade growths tend to occur in the younger group of women.

39. **Curtis H. Tyrone,** New Orleans, La.: **Operative Repair of Uterovaginal Descent.**—Operations for this condition were done as early as 1507, but not until much later were they generally performed. The author reviewed the various methods which have been employed for the treatment of uterovaginal descent. He discussed the application of the methods rather than the details of any particular operative procedure, although essential anatomy and brief descriptions of operative procedures were discussed. Prolapse may occur in virgins and in nulliparous women, but usually this condition is the result of prolonged labor. Indications for the employment of the interposition operation, the Manchester-Fathergill operation, and vaginal hysterectomy were reviewed. The author considered vaginal hysterectomy to be one of the most satisfactory operations, as it eradicates the associated cervical and endometrial disease. He also discussed the Le Fort operation, and spoke of the removal of the prolapsed cervical stump which may follow supravaginal hysterectomy.

Discussion: **Edward Richardson,** Baltimore, agreed that carcinoma of the fundus usually should be treated by means of radiation and surgery. He drew attention to the striking fact that there is a frequent time waste between the appearance of symptoms and the operative attack. If improved results are to be obtained in the management of this condition, such a time waste must be reduced. He reiterated the fact that no single operation is satisfactory for all cases of uterovaginal descent. **Emil Novak,** Baltimore, in addition to discussing the use of both radium and surgical methods in the treatment of carcinoma of the fundus, emphasized the importance of microscopic examination. Benign hyperplasia, although histologically quite distinct, is sometimes mistaken for adenocarcinoma. In the repair of cystocele it is important that the suburethral space be filled in or closed, and he referred to a triangular suture by which this might be accomplished. Perineorrhaphy does not cure rectocele, due to rectovaginal septum tears or stretching. **Donnell B. Cobb,** Goldsboro, N. C., spoke of postvaginal hernia and prolapse of the floor of the cul-de-sac of Douglas. This condition must be recognized and corrected if cure of the total condition of prolapse is to be accomplished. Unfortunately, almost half of the instances in which this condition exists are not recognized, although the diagnosis can readily be made by means of proper rectal examination. Treatment of this condition is similar to the treatment of other hernias. **John Burch,** Nashville, Tenn., discussed the occurrence of endometrial emboli following curettage. The employment of suction or punch methods permits diagnosis without the danger of dissemination of uterine carcinoma beyond its original location. He concurred with Cobb in his

belief that postvaginal hernia is more common than is generally recognized, and he advocated routine exploration of the cul-de-sac in cases in which vaginal hysterectomy is performed.

40. **Fred Krock,** Fort Smith, Ark.: **Arrhenoblastoma of the Ovary, Further Remarks.**—Only in recent years has it been fully appreciated that tumor tissue may function in a manner similar to its related normal tissue. To illustrate this point, the author cited the secretion of bile by a hepatoma which had metastasized to the brain. There are various types of arrhenoblastomas; some are associated with great, while others are associated with little, virilism, the variations in manifestations being related to the degree of differentiation of the tumor. The author reported further on a previously presented case in which femininity returned six weeks after the removal of the tumor. Subsequent operation, performed because of pain of which the patient complained, revealed two tumor nodules, and examination of the tissue removed at operation revealed cartilage in the recurrent growths. The theories which have been advanced to account for the occurrence of arrhenoblastomas were reviewed, and included the following: (a) hermaphroditism, (b) gonadal protective effect, (c) latent male elements, and (d) teratomas. The frequent finding of various types of cells in a single specimen supports the teratomatous theory. Other masculinizing ovarian tumors which the author considered in the course of his presentation included: (a) granulosa cell tumors, (b) aberrant cortical tumors, (c) embryonal carcinoma, (d) lutein cell tumors, (e) true sarcoma, and (f) dermoid tumors. Krock considered that arrhenoblastomas may represent one-sided teratomas.

Discussion: **Emil Novak,** Baltimore, remarked that Krock and his associates were the first observers in this country to describe arrhenoblastoma. In none of the three cases of his own, nor in the eight other cases in his laboratory, has Novak found evidence indicating a teratomatous nature of arrhenoblastoma. He believes that these tumors are related to the ovarian medulla or to the suprarenal cortex, both of which exert some masculinizing effects. Novak also remarked on the variation in the histologic appearance of arrhenoblastomas. Hirsutism alone is not an evidence or syndrome of masculinization.

REPORT OF THE MEETING OF THE ANESTHETISTS' TRAVEL CLUB, BOSTON, MASS., OCT. 7, 8, and 9, 1940

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EIGHTEEN members of the Anesthetists' Travel Club met in Boston Oct. 7, 8, and 9, with **Lincoln Sise, Philip D. Woodbridge,** and **Sidney Wiggin** as the hosts. Four members from Canada were able to attend: **Wesley Bourne** and **Charles Stewart,** from Montreal, and **Charles Robson** and **W. E. Brown,** from Toronto.

The mornings were spent at clinics at the New England Baptist, New England Deaconess, and Faulkner Hospitals. The outstanding anesthesia theme at all of these hospitals was undoubtedly the combined use of various anesthetics and methods to the advantage of the patient and the surgeon. Such combinations as intravenous and inhalation, spinal and inhalation, and spinal and intravenous anesthesia, were demonstrated with various types of cases as providing very adequate operative conditions together with the least unpleasantness to the patient and the least disturbance of his physiology.

In abdominal surgery, especially procedures upon the stomach and gall bladder, continuous or fractional spinal anesthesia was demonstrated. Some of these patients were also lightly anesthetized with cyclopropane or intravenous pentothal, barely into the zone of unconsciousness, to prevent tire and nausea. A very small additional dose of spinal anesthetic was occasionally added. Relaxation was excellent and controllable; general anesthesia, minimal. A hysterectomy was also performed under continuous spinal anesthesia. It was possible to start with a much smaller dose than would otherwise have been deemed necessary and the final total turned out to be less than would have been administered in a single dose.

Intratracheal cyclopropane was demonstrated for chest surgery, and intratracheal air-ether insufflation for brain surgery and major oral and head surgery.

Wiggin also especially stressed, in his clinical demonstrations at Faulkner Hospital, the combined use of spinal and other anesthetics in "balanced" anesthesia. In a seminar he presented a large number of anesthesia records, classified into groups, to demonstrate the control of blood pressure under spinal anesthesia and the management of anesthesia for bad-risk patients.

Tuesday afternoon was spent at Massachusetts General Hospital with **Henry K. Beecher** who demonstrated intratracheal ether-oxygen anesthesia for a pneumonectomy and led a round-table presentation and discussion on **Controversial Problems of Anesthesia for Thoracic Surgery.** Beecher advocates the use of ether rather than other anesthetics, and the attachment of a mask to the tracheal tube to provide a gas-tight connection rather than the use of an inflatable cuff or oropharyngeal packing. He advocates the former because of its margin of safety and the latter because of the desire for drainage of secretion around the tracheal tube in addition to aspiration through it.

Wednesday afternoon was spent at the Massachusetts Institute of Technology with **J. W. Horton** who has done a large amount of research on the explosion hazard. He demonstrated the explosibility of various mixtures of gases and showed that certain proportions of oxygen, ethylene, and cyclopropane, with the oxygen relatively high and the other gases in such proportions as to produce any

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plane of anesthesia, are noninflammable and will even quench a flame. No technique had as yet been worked out to insure the continuance of the mixture within the required limits in the actual clinical administration of anesthesia. Horton also demonstrated the prevention of accumulation of dangerous charges of static electricity by the use of metal intercoupling with interposed resistance and by the use of conductive rubber shoe soles, apparatus parts, and flooring.

At the Lahey Clinic Building on Monday afternoon the anesthesia staff presented an excellent program. Woodbridge gave their statistics for 1939. Sise reviewed intravenous anesthesia and gave many excellent points concerning the principles, precautions and management. **U. H. Eversole** and **F. H. Lahey** discussed postoperative bronchoscopic aspiration therapy. There was a symposium on all types of spinal anesthesia. In another discussion stress was placed upon the anesthetist's preoperative visit for the coordination of the preanesthetic medication with the patient's physical and mental status, the anesthetic to be selected, and the operation to be performed.

REPORT OF THE TWENTY-SIXTH ANNUAL MEETING OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA, CLEVELAND, OHIO, DEC. 2-6, 1940

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(From the Department of Radiology and Physical Therapy of the University of Minnesota)

THE annual meeting of the Radiological Society of North America was characterized by the attention given to matters of military interest. **W. Herbert McGuffin,** of Calgary, Canada, reported on a survey of recruits for the Canadian army, basing his observations on single film examinations of the chest of 10,000 enrollees. The chief interest centered about the basis of rejection and the classification of those examined. Recruits were placed in four classes: (1) those fit for full-time military service, (2) those fit for restricted military duty, (3) those fit for service in Canada alone, (4) those totally unfit for any military duty. Briefly, congenital, valvular, or hypertensive heart cases were placed in Class 4. Evidence of fibrotic tuberculosis under 21 years of age or of pneumoconiosis also placed the recruit in Class 4. Surgical or chest consultants are frequently called in to determine classification in more questionable lesions. Cases of active tuberculosis are not allowed to return to work in their respective communities without first undergoing observation and supervision, because of the potential menace to public health.

During the **Symposium on War-Time Roentgenology** which occupied one-half of a day's session, **Major Alfred A. DeLorimier** discussed in detail the new army portable x-ray equipment, with complete plans for x-ray service from evacuation units to the base hospital centers. Excellent apparatus has been designed and is being made, with the mobile units permitting complete fluoroscopic and film examination in conjunction with the surgical units. An efficient foreign body localization apparatus is a part of the x-ray setup and a demonstration of extremely rapid localization, as will be universally employed, was a feature of the army apparatus display. Since portable processing tanks have been perfected, complete

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film examination is available with all portable units. Present plans and equipment permit complete examination while the patient is on a stretcher, thereby avoiding moving of the wounded onto a table. Plans are being made for the use of low-voltage therapy in the evacuation or temporary centers. This may be an important adjunct to early surgical care of potential gas gangrene cases.

Roentgentherapy in Cancer of the Breast Used Preoperatively or in Non-operated Cases constituted the basis of a report by **Maurice Lenz,** of the Presbyterian Hospital, New York City. The possibility of complete cancer cell sterilization by this means appeared quite remote. Of 40 cases, 16 were shown to have distant metastasis at the time of surgery. A large number of cases, deemed surgically incurable, have received roentgen therapy alone, since survival rates probably are better than in those cases submitting to surgery even though admittedly incurable.

Late results in 33 cases of **benign giant cell tumors** of bone were reported by **Traian Leucutia,** of the Harper Hospital, Detroit. Eighteen cases had radiation therapy alone, and on the basis of the five-year end results this method was considered the one of choice. Disadvantages of surgical intervention are: (1) infection is not a rare surgical complication (it never occurred in the irradiated series); (2) filling in with bone after application of escharotics is often not satisfactory and reossification occurs faster in the irradiated group; (3) escharotics may act as irritants and result in late malignant degeneration. Most of the cases shown had good bone regeneration after a period of five to ten years and the anatomic and functional results were excellent. The method of therapy employed was that of repeated gradually decreasing doses, usually begun with a course of 525 r in air, with 200 kv. computed on the basis of a 20 by 20 cm. field. Usually 6 to 8 series, each dosage decreased by 10 per cent, extending over a period of two years, was employed. Especially good regeneration was noted in children. Restricted use of the extremity during treatment was recommended to obviate temporary bone decalcification, and possible secondary fracture. Discussants of the paper brought out the danger of not biopsying these lesions, since malignant sarcomas often mask the picture; also the danger of irradiating joints (epiphyses) of young children because of growth interference was emphasized. Cystic lesions about the knee joint were pointed out as being particularly prone to show malignant changes.

Paul A. Zahl, of the Memorial Hospital, New York City, discussed his experimental studies on the **localization of lithium-containing dye** in certain tumors in mice after intravenous injection. Since lithium atoms release tremendous energies, for surpassing the ionizing power of the electron, and since this violent release of energy occurs when the lithium atom captures "slow neutrons," the use of slow neutrons on lithiated tumors has been considered from the therapy standpoint. Analysis of the injected mice showed twice the concentration of lithium in the tumors as compared to surrounding normal tissue. Theoretically this will permit the release of three times as much energy in the tumor as in the normal tissue. One of the difficulties encountered has been the production of a high enough differential concentration of lithium between tumor and normal tissue; as a result the destructive effects cannot be localized to the tumor, unless it is in a readily accessible location. Another difficulty may also be encountered in obtaining proper slow neutron concentrations in the tumors.

The Metabolism of Radioactive Phosphorus by Malignant Neoplasms in Human Beings formed the basis of a report by **John M. Kenney,** also of the Memorial Hospital, New York City. Small "tracer doses" of radioactive phosphorus, orally administered, have been given to patients with lymphosarcoma, inoperable car-

cinoma of the breast, and osteogenic sarcoma of bone. After five to seven days, biopsies were made of the lesions; the percentage of the phosphorus retained in relation to the amount given, after deducting 25 per cent for loss of excretion, was calculated. This again was reduced to terms of "equivalent roentgens" present in the particular tumor. In certain cases as high as 1,000 to 1,500 equivalent r could be demonstrated in the nodes of lymphosarcoma. Sizeable doses were also demonstrated in metastatic nodes of inoperable carcinoma of the breast. Osteogenic sarcoma apparently absorbed more than any other tissue, and it was stated that it may be possible to give from 3,000 to 4,000 equivalent r to the tumor and lymph nodes. What effect this would have on the patient was not stated, since the amount of radioactive substance that may be tolerated by the body as a whole is as yet speculative.

Carleton B. Pierce, Montreal, Canada, described a new roentgen finding which indicates the presence of **fat and hemorrhagic fluid in certain traumatic fractures about the knee.** In the supine lateral position a fluid level was demonstrated with what appeared to be gas above the fluid level. There was no evidence of skin puncture. Further investigation showed a fracture of the head of the tibia with liberation of fat from the bone marrow, producing a layered shadow over the hemorrhagic fluid. Accordingly, in lateral films made in the supine position this layering phenomenon is due to fat and fluid in the bursae and indicates the presence of an intra-articular fracture, even though the fracture line itself may not be visible.

A symposium on **Methods in Irradiation Treatment of Carcinoma of the Cervix Uteri** was participated in by **R. R. Newell,** Stanford University, **R. S. Stone,** University of California Medical School, and **S. T. Cantrel,** Seattle, Wash.

In Stage I (League of Nations) lesions, if and when a case can be so classified, radium alone was recommended. Stone suggested surgical removal later if the case is operable. In the remaining stages (II, III, IV) external high voltage irradiation followed by radium application was generally agreed upon. It was emphasized that preliminary external irradiation was primarily designed for parametrial involvement. The advantage of using x-rays first was attributed to the favorable effect on infection and hemorrhage and to the reduction in size of the tumor and cervix, thereby permitting more effectual radium application. In all instances radium was relied upon to control the primary cervical lesion, but was not considered effectual for the parametrial region. The great danger of error in classifying Stage I cases (lesion localized to cervix) was pointed out by Stone; he quoted Taussig's operative figures wherein 25 to 33 per cent of so-called Stage I cases were found to have metastatic node involvement. Likewise, in Stage II and III cases 45 to 50 per cent and in Stage IV cases 66 per cent had node involvement. The iliac and hypogastric nodes, obturator, ureteral, and sacral nodes may be considered primary and the more distance nodes as secondary. Five to twenty per cent of cases may have primary node involvement without any evidence of parametrial spread, and in 5 to 10 per cent of Stage I and II cases, there may be secondary node metastasis without evidence of primary node involvement. However, 90 per cent of Stage I and II cases have metastases limited to the primary lymph nodes. A proper selection of fields of irradiation includes all these areas so that in a full course of therapy these regions receive the maximum effect permissible and the highest salvage possible may logically be expected. The necessity for individualization of treatment in each case was stressed by the essayists and discussants. The interval between completion of external irradiation and radiation application received some consideration. Suggested intervals varied from "a few days" to within "a period of two weeks." If too long a period elapsed, the possibility of development of radioresistance due

to fibrosis and tumor bed changes was emphasized. The more beneficial effect from radium applied after the external irradiation may be due to removal of infection in the cervix, since the presence of infection may produce a lessening of the degree of radiosensitivity of the tumor. Radium application by means of intracervical capsules and tubes in the fornices (colpostat) simultaneously in all possible instances appeared to be a recognized and preferable practice. **Axel N. Arneson,** St. Louis, indicated his best results were obtained in cases having had radium needle insertion and external irradiation applied simultaneously.

Max M. Peet, University of Michigan, discussed his experiences with **ventriculography in brain tumor diagnosis.** He stressed the value of determining the extent, location, and approximate size of the lesion, and indicated that this procedure is used in almost every case of brain tumor. A single posterolateral approach was advocated rather than the usual bilateral posterior trephining, and oxygen has replaced other substances as a contrast medium.

Gilbert Thomas, Minneapolis, Minn., emphasized the need for repeated bilateral retrograde pyelograms in the **diagnosis and treatment of early renal tuberculosis.** In most cases, because of the difficulty in proper preparation of the tuberculous patient, intravenous urograms are unsatisfactory for detecting the early lesion. The frequency of diffuse lesions by hematogenous spread means that the kidney should always be considered with suspicion in the presence of other distant lesions, such as bone or joint tuberculosis. A single negative pyelographic study does not rule out renal tuberculosis.

Claude S. Beck, Cleveland, Ohio, presented a cinematographic demonstration of lesions producing **compression of the heart,** in addition to his discussion of that subject. He prefers to class heart lesions in two large groups: extrinsic and intrinsic lesions. In extrinsic lesions, if the abnormality can be surgically corrected, the patient may be cured. Three chief extrinsic lesions producing interference with heart function as revealed by the pulse and blood pressure are: (1) angulation by adhesions, (2) torsion or rotation (dislocation), and (3) compression by fluid or scar tissue. His discourse concerned itself primarily with compression of the heart by scar tissue. Objection to the term ''adhesive pericarditis'' was voiced, since adhesions to the heart do not compress the heart, and in Beck's opinion do not in themselves interfere with heart action. Constrictive pericarditis or scar tissue, which may form on any chamber or chambers, results in actual compression, decrease in volume capacity, and in a characteristic and unmistakable clinical picture. The outstanding features are a small, quiet heart, evidence of venous pressure elevation and widespread pressure congestion (enlarged liver and spleen, ascites, edema, distention of veins of neck). A number of cases were demonstrated, the spectacular surgical procedures shown very clearly by means of motion pictures taken during the operations, and the final end results demonstrated on patients who have long since returned to work. Postoperative external drainage is not attempted.

Diaphragmatic Hernia of the Stomach was discussed by **David Beilin,** of Chicago. He stressed the increasing frequency of diagnosis and pointed out the importance of differentiating the true paraesophageal hernias from the true diaphragmatic congenital defects (foramina). These are often best shown in the lateral view. **George Crile, Jr.** (discussant), Cleveland, Ohio, pointed out that surgical repair is often not difficult; it is unfortunate that clinicians often do not consider surgical repair because of the impression that the surgical procedure is, in their minds, a formidable one. Crile believes the transpleural approach is usually not necessary. The ''short esophagus'' must be ruled out before contemplating surgery.

William S. Altman, of Beth Israel Hospital, Boston, pointed out the value of **Fractional Cholangiography** in both immediate and postoperative roentgen examination of the common duct. He recommended the use of 3 to 5 c.c. of diodrast (40 per cent) with films made either on the operating table or later in the x-ray department. After an interval of ten to fifteen minutes a second injection, through the catheterized common duct, of from 10 to 15 c.c. is made, and films are again taken. The preliminary small injection often demonstrates filling defects that are obscured by larger amounts of dye, and similarly filling defects may be conclusively demonstrated with the larger amount that were indefinite with a small amount. In 78 per cent of cases this fractional method of dye injection has been of distinct value. The sphincter of Oddi appears to be best demonstrated with the small injection. Caution should be exercised in exerting pressure during injection, since spasm of the sphincter may be induced. Amyl nitrite inhalation is of value in determining temporary spasm, since relaxation commonly follows its inhalation.

Clinical and Roentgen Manifestations of Gastrocolic Fistulas was discussed by **Max Ritvo** and **E. J. McDonald,** of Boston. While the clinical picture often suggests the diagnosis, the roentgen demonstration of the fistulous tract by means of the barium meal or barium enema examination constitutes conclusive diagnostic evidence. The importance of an early conclusive diagnosis was stressed since the mortality is high unless prompt surgical intervention and correction supervenes.

The need for prompt recognition of the fact that **Intrathoracic Neurofibromas** are often benign, usually surgically removable lesions, which do not respond to irradiation therapy, and are first detected by means of posteroanterior and lateral roentgenograms of the chest, was stressed by **Karl Kornblum** and **Howard H. Bradshaw,** of Jefferson Medical College, Philadelphia. These lesions, which are usually closely associated with the spine and represent a frequent posterior mediastinal tumor, can often be conclusively demonstrated in chest film examinations, which is the most important single diagnostic procedure. He stressed the constancy of their posterior position. They may become malignant and should be extirpated completely whenever possible.

Adrenal Tumors and the Use of Air Insufflation in Diagnosis was discussed by **Dr. George F. Cahill,** of New York City. Two hundred cases having symptoms of adrenal tumor, in which air insufflation of the pararenal fascial space was done, were reported. By means of this contrast method, Cahill was able to demonstrate that the vast majority of these cases were not due to adrenal tumors. Large carcinomas of the cortex were clearly demonstrated in certain cases and smaller hormonal secreting tumors of the cortex were also shown. In the hormonal medullary tumors diagnosis even with air insufflation was difficult because of their slight density and the occurrence of the tumors in the ganglia outside the adrenal. The author reported no accidents due to air insufflation, but emphasized the possibility of accident if air insufflation is done in the large tumors in which extensive dilatation of veins is present. During the discussion it was brought out that a number of fatalities have resulted from air embolism following insufflation, but Cahill felt that these were due to poor selection of cases.